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THE PROPHYLAXIS OF SUBACUTE BACTERIAL ENDOCARDITIS*

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SUBACUTE bacterial endocarditis consists essentially of a bacterial infection superimposed on previously damaged heart valves or on a congenital cardiac anomaly. The condition formerly was almost invariably fatal but treatment with penicillin and other antibiotic agents now results in the cure of 75 per cent or more of all patients. Certain cases, however, fail to respond, and in others serious or fatal congestive heart failure develops during the course of treatment or within a few weeks after completion of antibiotic therapy. It is important, therefore, that everything possible be done to prevent the occurrence of the disease.

It is known that dental extractions often are followed by transient bacteremia[1] and that in persons with rheumatic valvular disease or congenital cardiac anomalies, this not infrequently results in the development of subacute bacterial endocarditis. There is evidence also that the incidence of bacteremia can be reduced appreciably by the administration of penicillin prior to extractions.[1] Several observers have recommended that all patients who have rheumatic or congenital heart disease and who require dental extraction, tonsillectomy or irrigation of nasal sinuses receive penicillin as a preventive measure against the development of bacterial endocarditis. The present study was undertaken to ascertain what additional situations may be considered indications for the use of antibiotic agents for this purpose.

Material and Results

A series of 111 consecutive cases of subacute bacterial endocarditis was analyzed with particular reference to the type of pre-existing heart disease and to the event that appeared to have afforded entry of the infecting organism into the circulation. Rheumatic valvular disease was present in 100 patients, a congenital cardiac anomaly in 9, and syphilitic aortitis with aortic insufficiency in 2 (table 1). Only 59 of the 100 patients with rheumatic heart disease reported having been aware of the presence of a cardiac abnormality before the onset of bacterial endocarditis. In all of the 9 persons with congenital heart disease, however, the existence of the condition was known.

The portal of entry of the infecting organism and the event which made the portal available could be identified with reasonable certainty in 32 of the 111

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Table 1

TYPE OF PRE-EXISTING HEART DISEASES IN 111 CONSECUTIVE CASES OF SUBACUTE BACTERIAL ENDOCARDITIS

Type of Heart Disease	Number of Cases
Rheumatic valvular disease	100
Congenital cardiac anomaly	9
Syphilitic aortic insufficiency	2

cases (table 2). In all of these, blood cultures yielded growths of Streptococcus viridans or nonhemolytic streptococci. Dental extractions had been performed within 1 month of the onset of symptoms in 13 patients, the largest single group. The average time between the extractions and the first awareness of symptoms was 12 days. In 9 cases an acute infection of the upper respiratory tract had preceded the appearance of symptoms by an interval of 2 days to 2 months. The infections included acute tonsillitis, acute nasopharyngitis, acute pansinusitis, influenza, and acute bronchitis. In several patients in this group there had been no interval of apparently normal health between the original infection and the onset of symptoms attributable to infective endocarditis.

Two cases of subacute bacterial endocarditis followed criminal abortion, and a third began after spontaneous abortion in the seventh month of pregnancy. In one patient the initial symptoms occurred during the first week after normal delivery at term.

There were 3 cases in which subacute bacterial endocarditis developed after trauma to the skin or scalp with secondary infection. These included one instance of infected laceration of the scalp, one of severe cellulitis of the foot following the removal of a callus from a toe, and one of pyogenic skin infection about the site of a lumbar puncture. In this group, symptoms of systemic infection first became noticeable from 1 to 3 weeks after the trauma.

There was one case in which bilateral purulent otitis media immediately preceded the onset of symptoms.

In one patient the illness began during the second week after tonsillectomy and in another shortly after cholecystectomy.

In addition to the patients in whom the development of bacterial endocarditis could be causally related to some earlier event or infection, there were many whose dental hygiene was poor or who gave a history of chronic bronchitis, chronic sinusitis, or repeated attacks of tonsillitis. These conditions undoubtedly afford portals of entry at times for organisms causing subacute bacterial endocarditis but there was nothing to incriminate them in the clinical histories reviewed in the present study.

Discussion

The insidiousness of the onset of subacute bacterial endocarditis and the fact that bacteria may enter the blood stream through insignificant lesions without producing detectable evidence of local tissue damage make it impossible, in a majority of patients, to identify the route by which the organisms enter the circulation and the exact time at which invasion occurs. The results of the present study confirm the importance of dental extractions as a predisposing cause for the development of the disease. They indicate also that acute infections of the upper respiratory tract, acute otitis media, abortion, labor, and surgical or infected wounds may afford a portal of entry for the invading organisms. This mixed group and the group of dental extractions were responsible for nearly 30 per cent of the cases of subacute bacterial endocarditis analyzed. It seems apparent, therefore, that in individuals who have rheumatic valvular disease, congenital cardiac anomalies or syphilitic aortic insufficiency, dental extractions and the other conditions mentioned are indications for the routine employment of appropriate prophylactic measures. Further studies may identify additional situations in which preventative treatment should be carried out.

Not every person who has rheumatic valvular disease or some other cardiac abnormality which makes him a candidate for subacute bacterial endocarditis develops the disease after dental extractions or one of the other predisposing conditions. Data are not available as to the absolute frequency with which the combination of suitable cardiac soil and a potential avenue for admission of bacteria into the circulation results in the disease. Because of this it will be difficult to ascertain the efficacy of any program of prophylaxis. All that one can do is to suggest procedures which, in the light of our present knowledge, appear to be of promise. It must be emphasized that failure of subacute bacterial endocarditis to develop in a patient who has received preventive treat-

Table 2

PRECIPITATING FACTORS IN 32 CASES OF SUBACUTE BACTERIAL ENDOCARDITIS

Precipitating Factor	Number of Cases
Dental extractions	13
Acute upper respiratory infection	9
Abortion	3
Trauma to skin or scalp with secondary infection	3
Spontaneous labor at term	1
Purulent otitis media	1
Tonsillectomy	1
Cholecystectomy	1

ment cannot be interpreted as proof of the value of the measures employed. On the other hand, the occurrence of the disease in spite of prophylactic therapy immediately indicates a deficiency in management. Instances of this kind will occur, in all probability, and it would be of value if there were a central registry to which they might be reported. The information gathered in this manner would save time in identifying defective schedules and help in establishing more reliable methods of prevention.

Formerly it was our practice to carry out prophylactic therapy, in patients who were to have dental extractions or tonsillectomy, by the intramuscular administration of penicillin in doses of 50,000 units every 2 hours, beginning approximately 1 hour before the procedure and continuing for the subsequent 5 days. More recently procaine penicillin G in water or oil has been employed by intramuscular injection. Three hundred thousand units are given 1 hour before the extractions or tonsillectomy, and daily doses of the same amount are administered thereafter. The same schedule is followed in the presence of acute upper respiratory infections, infected wounds, abortion or childbirth. Treatment is continued for 5 days and for a longer period if fever persists. The recommendation that the minimum period of therapy be 5 days is an arbitrary one, and further experience may demonstrate that shorter courses, as advocated by Rhoads,[2] are adequate. In a series of 18 patients in whom prophylactic treatment has been carried out according to these schedules, there has been no instance in which subacute bacterial endocarditis has occurred. Other antibiotic agents, such as aureomycin and terramycin, may prove to be effective preparations for prevention of the disease.

There is one additional point to be commented upon. In the present series of cases, only 59 of the 100 patients who had rheumatic valvular disease reported knowing of the presence of a cardiac murmur before the onset of subacute bacterial endocarditis. This indicates a need either for a broader program of physical examinations, especially in children and young adults, or for giving patients more specific information about the presence of murmurs due to organic valvular disease. Persons who have congenital cardiac anomalies appear to be aware of their condition more commonly than do individuals who have the less severe grades of rheumatic heart disease. Certainly every patient who has valvular disease or a congenital abnormality of the heart or great vessels should be informed fully of the possible danger of dental extractions and the other conditions which may afford a portal of entry for subacute bacterial endocarditis and should be impressed with the indications for prophylactic antibiotic therapy.

Summary

The portal of entry of the infecting organism and the event which made the portal available were identified with reasonable certainty in 32 of 111 consecutive cases of subacute bacterial endocarditis. In 13 patients, dental extractions had preceded the onset of the illness, and in 9 others, there had been an earlier acute infection of the upper respiratory tract. The disease followed

abortion in 3 instances and began during the first week post partum in 1. Three cases occurred after trauma to the skin or scalp with secondary infection, and in 1 patient bilateral purulent otitis media immediately preceded the onset of symptoms. One case began after tonsillectomy and another after cholecystectomy.

In view of these findings it is recommended that all patients who have valvular heart disease or a congenital cardiac anomaly be given procaine penicillin G in water or oil by intramuscular injection (1) before and for 5 days after dental extractions or tonsillectomy, (2) during acute infections of the upper respiratory tract for a minimum of 5 days and longer if fever persists, (3) before spontaneous or therapeutic abortion and spontaneous or induced labor and for the following 5 days, longer if fever is present, and (4) in the presence of infected wounds for a minimum of 5 days or until all evidence of local infection has cleared. Further studies may identify additional situations in which preventive treatment should be employed. Other antibiotic preparations may also prove to be effective prophylactic agents.

The difficulty of determining the efficacy of a program for preventing bacterial endocarditis has been emphasized. Instances of failure to protect against the disease will point the way to more effective procedures. A central registry to which such cases might be reported would hasten progress.

It is important that patients be informed of the presence of valvular heart disease or a congenital cardiac anomaly and of the indications for prophylactic measures against subacute bacterial endocarditis.

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PULMONARY HAMARTOMA

Report of Three Cases

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HAMARTOMA has been described in most organs of the body. Earliest recognition of this tumor is credited to Chiari[1] in 1833. Albrecht,[2] in 1904, described a vascular tumor of the liver, and suggested the term "hamartoma" or "error tumor." In so doing, Albrecht proposed the concept of a tumor formed by the normal tissue elements expected in that location. The term "reduplication cyst" has also been used to indicate a growth whose tissue elements are abnormal only in their quantitative value.

The hamartoma is not always a vascular neoplasm. In the lung this tumor usually is composed of bronchial elements including cartilage, muscle, fat, and mucosa. The bronchial hamartoma is ordinarily a solitary parenchymal lesion but may appear as a pedunculated, endobronchial growth. The latter type is rare; less than 15 case reports are found in the literature.[3]

Incidence

Hamartoma of the lung is an uncommon tumor. Many are described as incidental postmortem findings which apparently had produced no clinical symptoms. Johnson and Clagett[4] report 2 hamartomas in a series of 384 lung resections of all types, an incidence of 0.5 per cent. Effler and Blades[5] list 1 hamartoma in a series of 24 resected solitary lung tumors which were asymptomatic.

The endobronchial hamartoma is extremely rare. Postlethwait and Hagerty[3] collected 12 cases in the world literature and reported 1 of their own. Nine of these were detected clinically, while 3 were discovered at autopsy.

Etiology

The etiology of pulmonary hamartoma is not understood. A summary of the etiologic concepts reviewed by Branchi and Etchegoyen[6] includes 4 groups: 1. congenital malformation; 2. hyperplasia of normal structures; 3. neoplastic origin and 4. inflammatory origin.

In general, it appears that this tumor is developmental in inception and arises in misplaced bronchial anlage. Some authors[7] call attention to the fact that anthracosis has never been observed in this lesion despite the fact that it may be present to a noticeable degree in the surrounding parenchyma. Jones[8] described a large hamartoma in a newborn infant. It has been emphasized[9] that the lungs develop by a process of budding from the primitive bronchi with

the most primitive areas at the periphery. The columnar epithelium of these primary bronchi is surrounded by the membrana propria or basement membrane. This layer forms the connective tissue framework of the lung; muscle and cartilage develop from the fetal epithelium. It has been postulated that localized changes in the arrangement, quantity or differentiation of bronchial components could produce the hamartoma.

Clinical Findings

The peripheral hamartoma rarely manifests itself except as an unexpected finding on the chest film. The radiographic appearance is that of a solitary "coin lesion" and is indistinguishable from tuberculoma, solitary metastasis,

FIG. 1. Endobronchial hamartoma. Cut section through left main stem bronchus.

bronchogenic cyst, or any other lesion that may produce a spherical density in the lung field. In recent reports, Hall[10] and Bragg and Levene[11] have suggested that the diagnosis of hamartoma may be suspected in so-called "coin lesions" which have spicule-like dispersion of the calcium.

Endobronchial hamartoma is manifested by the symptoms of bronchial irritation and obstruction and clinically is indistinguishable from the bronchial adenoma, fibroma or polyp. The symptoms may be insidious in onset and intermittent in character. Usually there will be cough, hemoptysis, fever, fatigue, weight loss and chest discomfort. The patient may cough up fragments of necrotic tumor. The radiographic studies of the chest usually are compatible with obstructive pneumonitis or atelectasis.

Case Reports

Case 1. A 56-year-old patient presented a history of cough, hemoptysis, and febrile episodes, for a period of 1 and ½ years. The cough was persistent and productive of mucoid sputum. There had been 2 major pulmonary hemorrhages, 1 of which resulted in an emergency hospitalization.

Initial examination in the Cleveland Clinic revealed a well developed Negro who did not appear ill. Physical examination and laboratory studies were noncontributory. Radiographic studies, however, were significant, and the diagnosis of left upper lobe atelectasis was made.

Endoscopic examination revealed an intrabronchial mass protruding from the left upper lobe orifice. It appeared to be polypoid in nature and was covered in part with mucosa. A biopsy was obtained and the impression of benign tumor was recorded.

Thoracotomy was performed on December 12, 1949 and the clinical impression of upper lobe atelectasis confirmed. Extensive inflammatory reaction made total pneumonectomy mandatory. The postoperative period was uneventful, and the patient has remained symptom-free to date.

Examination of the specimen (fig. 1) revealed a pedunculated mass arising from the left upper lobe bronchus. The growth which was 1 cm. in diameter and 2 cm. in length completely occluded the upper lobe bronchus. The microscopic examination revealed a central core of fat, cartilage and collagenous connective tissue surrounded by respiratory epithelium. The cartilage was distributed in bar-like arrangement and had a well-defined perichondrium. At the base of the lesion this cartilage appeared to

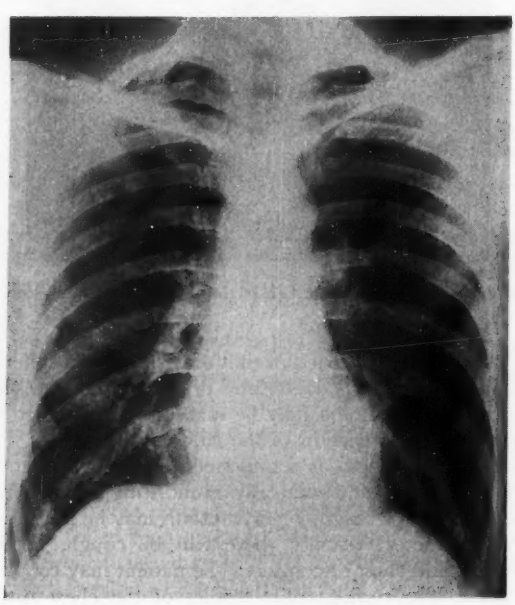


FIG. 2. Case 2. "Coin lesion" in left lower lung field.

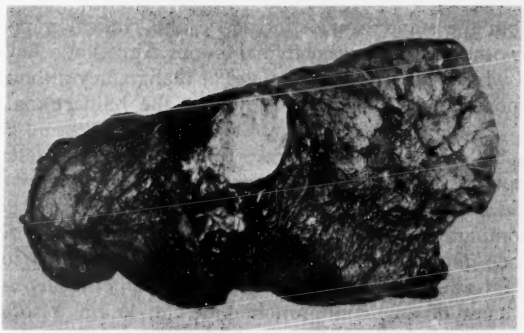


FIG. 3. Case 2. Cut section of left lower lobe revealing well-circumscribed peripheral hamartoma.

be continuous with the cartilage beneath the mucosa of the normal bronchus. There was no evidence of malignancy.

Case 2. A 45-year-old patient was examined at the Clinic on October 10, 1949 because of rectal bleeding. Internal hemorrhoids were observed and surgery advised. The routine chest survey revealed a "coin lesion" in the lower left lung field (fig. 2). There were no symptoms of pulmonary disease.

The tumor was removed by lobectomy a week subsequent to examination. The patient recovered promptly, and on the eighth postoperative day the hemorrhoidectomy was performed.

The gross examination of the resected tumor revealed a firm mass in the central portion of the lobe (fig. 3). On cut section the tumor measured 3 cm. in diameter and presented a mottled yellow appearance. It was firm in consistency and there appeared to be islands of cartilagenous material. On microscopic examination, nests of hyaline cartilage predominated and were imbedded in loose connective tissue. Smooth muscle, fat and epithelial lined spaces were also distributed in the stroma.

Case 3. A 56-year-old man was referred to the Clinic for treatment of diabetes mellitus. Roentgen examination of the chest revealed a solitary lesion in the left upper lobe that appeared uniform in density, spherical in contour and the size of a ping-pong ball (fig. 4a). There were no associated localizing symptoms. The clinical impression was either tuberculoma or peripheral bronchogenic carcinoma.

A left upper lobe lobectomy was performed on October 12, 1950. The mass seemed to be centrally located in the parenchyma of the lung. Resistance was encountered when cutting through the thick gristle-like mass which grossly consisted of white cartilaginous material dispersed in convolutions. Microscopic sections revealed broad islands of hyaline cartilage with narrow interspersed zones of loose connective tissue and small areas with cuboidal epithelium, plasma cells and occasional lymphocytes. The pathologic report was hamartoma, bronchial type (fig. 4b).

Discussion

Parenchymal hamartoma is usually a benign, asymptomatic lesion which is detected by radiographic survey. The diagnosis can only be made by tissue study obtained at operation or postmortem examination. The significance of

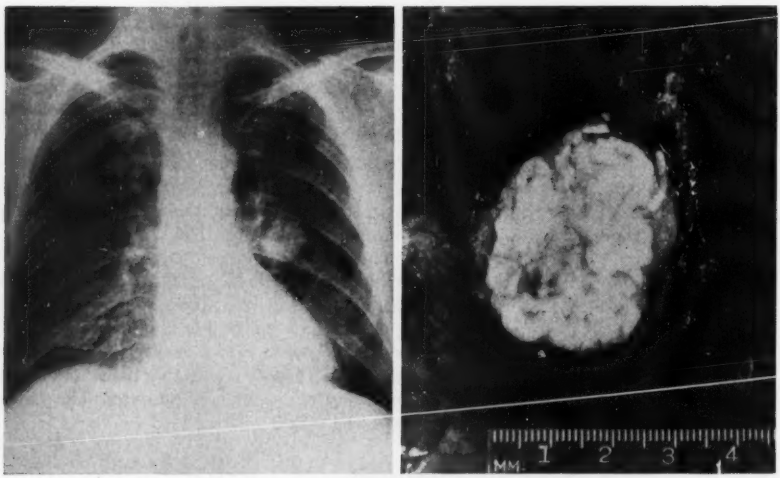
this tumor from the standpoint of incidence and clinical import is slight in comparison to other solitary parenchymal lesions. Simon and Ballon[12] reported a hamartoma which showed local changes of malignancy although metastases were not demonstrated. In general, however, the hamartoma is considered benign.

Endobronchial hamartoma is a rare tumor which manifests itself by obstructive symptoms; though a benign neoplasm, the resultant lung damage due to bronchial occlusion may be serious. Massive hemorrhage is a distinct possibility. Comparatively few of these interesting lesions have been described, nevertheless one questions their extreme rarity. Undoubtedly some of the so-called bronchial adenomata could be classified authentically as hamartoma.

The treatment of any endobronchial benign lesion is total extirpation. Endoscopic removal is indicated when residual lung damage is slight. If irreversible secondary pulmonary changes have occurred, some form of resection is indicated. In the cases collected by Postlethwait and Hagerty,[3] 5 tumors were removed endoscopically and 1 by lobectomy.

Conclusion

Pulmonary hamartoma is an interesting and rare tumor. Unless it is an endobronchial lesion, hamartoma is probably of slight clinical significance. Nevertheless, the surgical removal of all solitary asymptomatic lung tumors is generally advocated, and consequently more of these neoplasms will be discovered. Whereas the diagnosis of hamartoma may seem to be only of aca-



(a) (b)

Fig. 4. (a) Roentgenogram demonstrates discrete lesion in left lung. Lateral projection localized tumor in upper lobe. (b) Cut section of specimen showing the convolutions of cartilage within the tumor.

demic interest, the pathologic identity of the solitary lung tumor makes its recognition mandatory.

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HAMARTOMA OF PERICARDIUM — LYMPHATIC TYPE

Case Report

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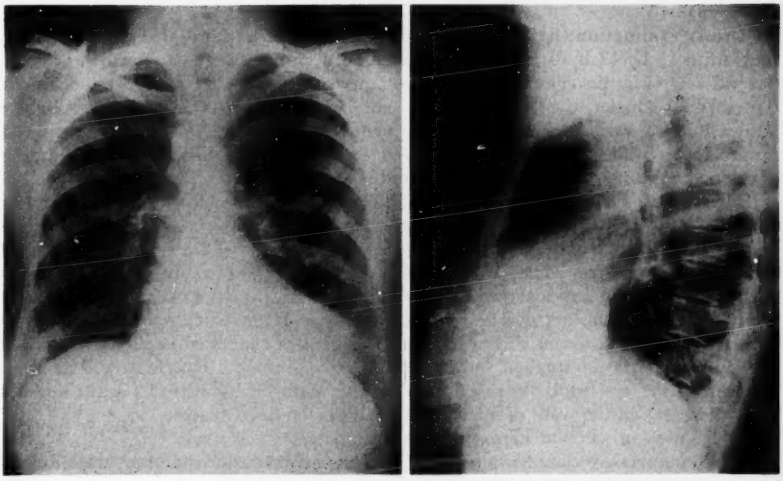
PRIMARY neoplasms of the pericardium are rare. Yater[1] in a comprehensive review of tumors of the heart and pericardium in 1931 mentioned lipoma, sarcoma and mesothelial tumors as the types encountered. He also presented a cyst "probably of a lymphatic vessel" in the pericardial fat at the apex of the heart. Histologic evidence, however, was lacking in his report. Keller and Callender[2] have described a large neurofibroma attached to the pericardium apparently originating from the phrenic nerve. A teratoma lying within the pericardial cavity and adherent to the pulmonary artery was noted by Joel[3] in 1890. More recently Greenberg and Angrist[4] have reported 2 cases demonstrating hemangiomatous tumors of the pericardium. One of these was of the benign cavernous type; the other a progressive, invasive angio-endothelioma.

Although lymphangiomatous cysts of the mediastinum are considered rare, reports of their occurrence have appeared occasionally in the literature. Stout,[5] in commenting upon N. C. Foot's discussion of mediastinal tumors, emphasizes the occurrences of such lesions. Although many of the cases of mediastinal lymphangiomatous cysts reported have demonstrated attachment to the pericardium as well as to other thoracic structures, their exact origin has not been established and histologic descriptions have been lacking in some instances. In the foreign literature in 1929, Eliaschewitsch[6] reported an example of cystic lymphangioma arising on the posterior surface of the pericardium. Lenkeit,[7] a year previously, observed a cyst on the anterior surface of the heart but its true nature was not discussed.

Analogous cases of cystic lymphangioma arising anatomically from the pericardium and proved by histologic examination to have been of lymphatic origin have not been recorded in the American literature which we have reviewed. The symptoms produced by this lesion, in addition to its fundamental rarity, suggest the individuality of the subsequent report.

Case Report

A 38-year-old white woman was referred to the Cleveland Clinic Hospital for treatment with a roentgenographic diagnosis of tumor of the lower lobe of the left lung. The



(a) (b)

FIG. 1. (a and b) Anteroposterior and lateral roentgenograms of chest demonstrating mediastinal lesion.

patient however, denied all symptoms referable to the respiratory system. Her only complaint was that, on change of position, she experienced a sensation of "something flopping about in the left chest." This condition had been present for approximately 10 years.

The past medical history revealed extensive rib fractures of the left thorax which had been experienced 17 years previously.

The patient was well nourished and appeared neither acutely nor chronically ill. Examination of the heart and lungs was negative. The blood pressure was 130/90. The pulse rate was 80 per minute and regular. No mediastinal shift was demonstrable. Examination was otherwise normal.

A laboratory examination revealed 4,210,000 red blood cells, 11.0 Gm. hemoglobin and 6150 white cells with a normal differential count. The urinalysis and blood chemistry determinations disclosed no abnormalities.

Roentgenologic studies of the chest (fig. 1 a and b) revealed an area of increased density approximately 10 cm. in diameter just above the left diaphragm, posterior to the sternum and adjacent to the left cardiac border. Healed fractures of the fifth, sixth, seventh and eighth ribs on the left side were evident.

Because of the previous history of trauma a hernia through the morgagnian foramen was considered as the most likely disgnosis, although the incidence of bronchiogenic or pericardial cyst could not be excluded.

A left exploratory thoracotomy was performed. A cystic structure was encountered adjacent to the left border of the pericardium; at one point, however, in direct contact with the pericardial sac. The cyst was somewhat mobile due to this pedicle. After sharp and blunt dissection the pedicle was ligated and divided and the cyst easily removed in toto.

Pathology

Gross examination (fig. 2). The specimen consisted of a triloculated cystic structure measuring 12 by 12 by 6 cm. A thin, glistening, richly vascular capsule was evident. Several tags of fat tissue were noted on the outer surface. The largest section measured 6.0 cm. in diameter, the others 5 and 3 cm. On rupturing, a clear, watery, slightly amber fluid was released from the compartments. The wall at its thickest part measured 3 mm. In the wall of the largest locule were three flat, dense, white areas. The lining of each compartment was finely nodular and reddish-yellow in color.

Microscopic examination (fig. 3 a and b). Sections revealed the cystic structures to be lined by endothelial cells. Smooth muscle, as well as dense collagenous connective tissue, was apparent within the walls. Beneath the endothelium were collections of lymphocytes which, in some areas, formed nodular aggregates. An occasional endothelial-lined blood-filled space was detected in the wall. Small spaces with peripheral lymphocytes were also noted. The outer surface of the cystic structure consisted of loose areolar and adipose tissues with a moderate number of congested capillaries. Sections stained by the Masson method verified the presence of smooth muscle as well as dense collagen in the cyst walls. Verhoeff elastic tissue stain demonstrated a scant amount of elastic tissue in the walls of a few of the endothelial-lined spaces.

A diagnosis of vascular hamartoma, lymphatic type, was made.

The postoperative course was uneventful. The patient was discharged 1 week following operation and has remained asymptomatic and in good health for the 2 subsequent months.

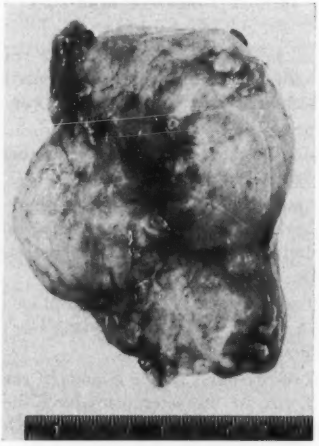
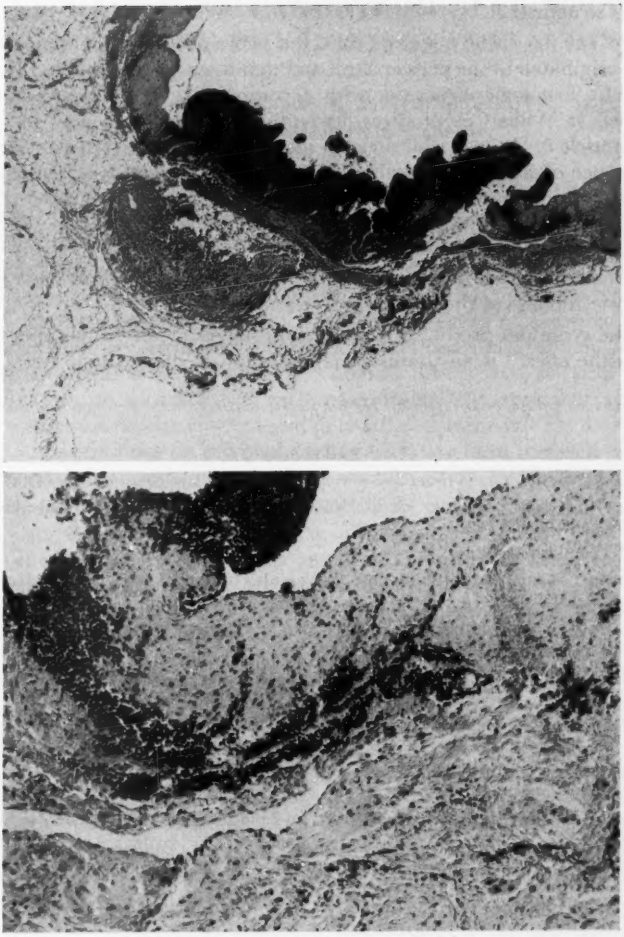


FIG. 2. Gross specimen. Note suture about pedicle.

Comment

Yater[1] has outlined the symptomatology of pericardial tumors. Many of the cases which he has reviewed do not present symptoms attributable to a mediastinal or pericardial lesion, their diagnosis usually resulting from an accidental finding following roentgen examination of the chest. The most out-

(a)



(b)

FIG. 3. (a and b) Low and high power photomicrographs of cyst wall. Note lymphocytes; collagen and smooth muscle, endothelial lined spaces.

standing symptoms of pericardial tumors have been those due to cardiac tamponade. In none of the reported cases of mediastinal cystic lymphangiomas by Skinner and Hobbs,[8] Michaelis,[9] Swift[10] and Sanes et al[11] have the symptoms described by our patient been indicated. This lesion is unusual in that it offered none of the technical difficulties so often encountered in the resection

of cysts of lymphatic origin; doubtless the result of their adherence to surrounding structures.

There can be little question that the thoracic cyst encountered in this instance originated in the pericardium and that it was predominantly lymphatic in type. Its histologic structure, with accompanying lymphocytic aggregates designates, as Willis[12] emphasizes, its lymphatic derivation. The inclusion of smooth muscle in the cyst wall suggests the hamartomatous nature of the lesion. The presence of small blood-containing spaces in the wall is a frequent observation in lymphatic cysts.

Conclusion

1. A case of pericardial hamartoma, lymphatic in type, has been reported with a brief review of the pertinent literature.

2. The symptom produced by the lesion suggestive of "something flopping about in the chest" is an unusual manifestation of mediastinal cyst.

The authors are grateful to Dr. John B. Hazard for his assistance in the presentation of this case.

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THE APPRAISAL OF CARDIOVASCULAR STATUS IN INFANCY BY PHYSICAL EXAMINATION

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ADVANCES in cardiovascular surgery have stimulated interest in the prompt appraisal of the functional significance of congenital cardiovascular defects. The demand for precise anatomic diagnosis has led to the utilization of complex diagnostic methods, such as cardiac catheterization, angiocardiography, fluoroscopy, respiratory gas analysis, and simultaneous precordial lead electrocardiography. Initially, however, recognition of the presence of an anomaly, estimation of its functional importance, and an attempt at accurate localization depends on the patient's history and physical examination. This can be accomplished with some degree of exactness in the case of the more common defects encountered in childhood and adult life. In infancy evaluation of the findings on physical examination has been less well defined, and a correct anatomic diagnosis rarely is established on this basis alone.

The highest mortality rate in congenital heart disease occurs in infancy. One reason for this is that certain defects are so severe as to be incompatible with extra-uterine life. Nevertheless a significant number of deaths occur in infants having anomalies which are either relatively benign, when encountered in older age groups, or are amenable to surgery. In a series of 110 postmortem examinations on children with congenital heart disease who died before the third year of life, Marquis[1] noted that 25 per cent of the total group had ventricular septal defects. Deaths due to severe tetralogy of Fallot or to uncomplicated patent ductus arteriosus in the first year of life are not uncommon.

If the mortality and morbidity of congenital heart disease in infants is to be reduced significantly, an early estimate of the functional status of the cardiovascular system must be made. This can be determined on the basis of symptoms and physical findings by (1) recognition of any existing cardiovascular anomaly at the earliest possible age, and (2) prompt functional classification of the nature and severity of the lesion by evaluation of changes evident in the heart and circulation. This approach will provide a reasonable basis for the prompt institution of medical management, intelligent selection of further diagnostic studies, and timely utilization of available surgical technics.

Symptoms which suggest the presence of a cardiovascular malformation are: tachypnea, persistent cough, frequent recurrence of pulmonary infections, cyanosis, syncopal attacks, stridor, growth failure, vomiting, and edema.

The possibility of such a malformation should be considered in any infant whose resting or sleeping respiratory rate persistently exceeds 60 per minute. Tachypnea appears whenever there is a fixed reduction in the volume of pulmonary blood flow due to the presence of an organic obstruction at the origin

of the pulmonary artery. It is also the earliest manifestation of pulmonary engorgement. The latter indicates a relative increase in the total blood volume in the pulmonary circulation. This condition occurs when there is myocardial failure, a mechanical obstruction to pulmonary venous return, or a large shunt of oxygenated blood into the right heart or pulmonary artery with a consequent significant increase in the volume of pulmonary blood flow.

Persistent cough is often a symptom of pulmonary engorgement which may be erroneously attributed to infection. Superimposed attacks of bronchitis and pneumonitis are common, and are recognized by the appearance of leukocytosis and fever. These infections respond to antibiotic therapy, but cough and tachypnea persist because of the abnormal circulation.

The presence of cyanosis is the best physical evidence of a shunt of systemic venous blood into the systemic arterial circulation. In severe myocardial insufficiency cyanosis may be present without a venous-arterial shunt. When anemia exists it is often impossible to exclude defects which are producing mild, or even moderately severe, systemic arterial oxygen unsaturation. Cyanosis is not visible unless there are 5 Gm. or more of reduced hemoglobin per 100 cc. of circulating arterial blood. If the total hemoglobin amounts to only 10 Gm., there must be more than 50 per cent arterial oxygen unsaturation before even minimal cyanosis appears. Cyanosis is caused by a great variety of defects which cannot be anatomically differentiated on the basis of physical findings. These may be classified however, into two groups on the basis of the presence or absence of pulmonary engorgement. Those presenting evidence of pulmonary engorgement seldom can be improved by operation, but those showing deficient pulmonary circulation usually are operable.

Obstruction to pulmonary blood flow, as seen in pulmonary stenosis, frequently causes syncope and at times convulsions. Less commonly these anoxic attacks occur in association with defects producing extreme pulmonary hypertension. Cyanosis increases during attacks, unless there is anemia, in which case a grayish pallor will be evident. These episodes are so characteristic of a severe obstruction to pulmonary flow that their occurrence justifies the clinical diagnosis of pulmonary stenosis, necessitating prompt definitive adjunctive studies.

Infantile stridor occasionally is caused by anomalies of the aortic arch system producing constriction upon the trachea and esophagus. When no cause can be found, a complete cardiovascular examination is indicated since early surgical correction is necessary in order to avoid prolonged pulmonary complications.

Failure to gain weight is apparent sometimes in cyanotic infants, but is encountered much more frequently in the noncyanotic group, when a large shunt of blood from the left to the right side of the heart results in a decreased systemic blood flow. Vomiting may occur because of partial esophageal obstruction or passive congestion of the viscera. The appearance of edema in infants, when due to congestive failure, usually is made evident by periorbital swelling.

The cardiovascular examination of infants should be an orderly and systematic procedure. Unfortunately, examination of the newborn infant is too frequently conducted in or near the bedlam of the nursery, where precise auscultation is often impossible. In our experience most pathologic heart murmers have not been recognized until the baby is 4 to 6 weeks of age, when the examination usually is conducted under more favorable circumstances. The responsibility of assuring the normalcy of a newborn infant should justify the preparation of a satisfactory environment for examination. The only requirements are quiet, warmth, cleanliness, and adequate daylight. If the examination is done during the first hour after feeding, the problem of persistent crying is minimized. Chilling frequently causes a mottling of the skin, sometimes confused with cyanosis.

While the baby is resting or sleeping the rate and character of respirations and the presence of stridor should be noted along with the state of hydration and nutrition. Cyanosis and any evidence of clubbing of the fingers should be observed. A precordial bulge may be recognized on inspection. Gentle palpation over the precordium will assist in an estimation of heart size by localization of the apical impulse. If a thrill is present, its point of maximum intensity should be determined. A warm stethoscope should be used for auscultation, and sudden changes in its position or heavy pressure upon the chest avoided. Loud breath sounds may prevent precise identification of faint murmurs and abnormal heart sounds. Newborn infants, when at rest, have periods of apnea, which are advantageous if the examiner will wait for and utilize them. The heart rate is counted by auscultation. Careful palpation will reveal the existence of hepatomegaly or intrinsic pulsations in the liver. Abdominal aortic and femoral arterial pulsations should be compared with those of the radial arteries. Auscultation and percussion of the posterior chest is then performed with the infant in the prone position. If cyanosis has not been noted previously, crying should be stimulated, and any color changes in the skin evaluated. When performed in the manner described a satisfactory examination may be accomplished with minimal loss of time.

A systolic heart murmur is the most frequent reason for suspecting cardiovascular disease in infants. During the first 3 or 4 days of life one occasionally hears a grade 2 to 3 systolic murmur in an otherwise normal baby. Taussig[2] has attributed these murmurs to functional patency of the ductus arteriosus. The murmur disappears after a few days with functional closure of the ductus, which precedes complete anatomic obliteration by as long as 3 months. From 5 to 7 days after birth until the age of 6 or 8 months a grade 2 or louder systolic murmur almost invariably signifies a congenital cardiovascular malformation. One is never justified in assuming these murmurs to be physiologic in origin. Actually, because of the difficulties encountered in precise auscultation at this age a natural process of screening takes place and faint murmurs of transient occurrence, which would be classified as physiologic, rarely are recognized. During a study of 630 infants, Cox[3] found only 10 with systolic murmurs at any examination up to the age of 6 months. Of these, murmurs were incon-

stant in 6, suggesting an incidence of physiologic murmurs lower than 1 per cent in the group under 6 months of age. From 6 to 8 months physiologic murmurs appear more frequently and after 2 years are encountered in the majority of preschool children.

In infancy the auscultatory characteristics of a murmur are of little value in locating the defect producing it, or in appraising its functional importance. Almost all murmurs present before the age of 6 months are systolic in time. Because of the small heart size the point of maximum intensity of the murmur is difficult to locate, and the thin chest wall results in nonspecific transmission of the murmur throughout the chest. Systolic murmurs caused by anomalies resulting in cyanosis are indistinguishable from those produced by uncomplicated septal defects of patency of the ductus arteriosus. A septal defect without symptoms or cardiac enlargement may produce a murmur similar to that found in another infant with an identical, but larger defect which has caused functional disability.

Diastolic murmurs are seldom heard during infancy. When audible, however, they are less intense and more readily localized than are systolic murmurs. Of particular importance is a short, late, rough diastolic murmur, most audible medial to the cardiac apex; this is detected in noncyanotic infants with cardiac enlargement and pulmonary engorgement. Its presence has often been associated with the development of myocardial insufficiency in this group of patients. In older infants a blowing, high pitched, early diastolic murmur, loudest in the second or third left interspace, may be due to pulmonary insufficiency in the presence of severe pulmonary hypertension. In a few instances a loud systolic murmur continuing into mid-diastole is encountered in the same area. This murmur is caused by a compensatory shunt of blood to the lungs when there is obstruction to flow at the pulmonary outflow tract, such as a naturally occurring patent ductus arteriosus in the presence of a tetralogy of Fallot. In infants a continuous or "machinery" murmur is never due to an uncomplicated patent ductus arteriosus, since the diastolic pressure difference between the systemic and pulmonary circulation is small. A few severe malformations occur without murmurs, and in these cases extreme cyanosis will direct attention to the cardiovascular system. A truncus arteriosus arising from a single ventricle may be responsible for this clinical picture.

Careful study of the heart sounds provides valuable information. If splitting of the second sound occurs, one may strongly infer that both aortic and pulmonic valves are present and capable of closure. This excludes those cyanotic defects in which one valve is absent or incapable of closure. When both valves are present and functioning, their closure may be synchronous, but careful repeated auscultation usually will reveal at least slight reduplication of the second sound. A third heart sound occurring in early or mid-diastole is heard in normal infants and often is accentuated in the presence of septal defects of sufficient magnitude to produce cardiac enlargement. This is more often the case in auricular than in ventricular septal defects.

In infancy, a bulging sternal deformity usually is evidence of enlargement of the right ventricular outflow tract. When this is perceptible in a cyanotic defect there is usually an associated increase in pulmonary blood flow. Conversely, those anomalies causing cyanosis and decreased pulmonary flow, such as tetralogy of Fallot, ordinarily do not show this specific type of enlargement, and sternal deformity is absent. The exception to this rule is valvular pulmonary stenosis with an intact ventricular septum. In this instance, the pulmonary outflow tract proximal to the pulmonary valve becomes enlarged, and despite a decreased pulmonary blood flow, precordial bulging occurs. Noncyanotic defects accompanied by large shunts of arterial blood into the pulmonary circulation also lead to enlargement of the pulmonary outflow tract, which condition is not caused by identical anatomic defects of smaller size. Thus, in noncyanotic lesions such as auricular and ventricular septal defects, and patency of the ductus arteriosus, one may roughly estimate the functional severity of the lesion by the presence or absence of precordial bulging. Generalized cardiac enlargement without eccentric hypertrophy of the pulmonary outflow tract may be recognized by displacement of the cardiac apex from its normal position in the fourth or fifth interspace at the left midclavicular line. This is estimated more accurately by palpation of the apical impulse than by percussion of cardiac dullness. Dextrocardia is easily recognized by this method.

Auscultation over the hilar areas and posterior lung fields may reveal persistent, fine, crackling inspiratory rales due to pulmonary engorgement. When this occurs in noncyanotic lesions, with an intracardiac left to right shunt, it implies major functional disability. In cyanotic lesions rales are absent if there is a reduced pulmonary blood flow. The significance of such rales can be evaluated only when pulmonary infection or atelectasis are excluded. Pulmonary edema is not observed in infancy except as a terminal complication.

Hepatomegaly and venous distention are early manifestations of congestive failure, and may exist for months before the appearance of dependent edema, ascites, or pleural effusion. Intrinsic or expansile pulsations in the liver may be caused by tricuspid atresia, or pulmonary stenosis with an intact ventricular septum, when there is only a small auricular septal defect allowing escape of venous blood from the right auricle. Anasarca, when due to congestive failure, is usually a terminal event.

The absence of pulsations in the abdominal aorta and femoral arteries makes possible the diagnosis of coarctation of the aorta in early infancy. When this anomaly is uncomplicated, its presence should always be recognized at the time of physical examination. In rare instances, when a patent ductus arteriosus empties its blood from the pulmonary artery into the aorta beyond the occluded segment, femoral pulsations may be felt. In such instances cyanosis usually is present in the lower extremities and absent in the head and arms.

Summary

The early recognition of cardiovascular malformations offers the best opportunity for lowering the mortality and morbidity caused by these defects

in infancy. This is primarily the responsibility of the physician entrusted with the routine examination and care of newborn infants. In this age group it is possible to recognize the presence of a cardiovascular anomaly and to make an estimate of its functional severity on the basis of symptoms and physical findings. The usefulness and limitations of the signs and symptoms most frequently encountered have been presented. Their recognition and evaluation provide the best foundation for medical management, intelligent use of more complex diagnostic methods, and the timely utilization of appropriate surgical technics.

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SOME SIMPLE INEXPENSIVE METHODS FOR DETECTION OF RADIOACTIVITY*

Training Citizens to Meet Possible Atomic Disaster

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THE recent article by Lauritsen and Lauritsen[1] describing a "radiation meter for disaster use" is a timely and valuable contribution. These authors call attention to the serious danger to body and mind of civilians who have no training or knowledge of radioactivity and are totally unprepared to meet the dangers of an attack by an atomic bomb or other military use of radioactive materials. They describe a small, relatively simple radiation meter based upon the principle of ionization in air, and calibrated in fractions of one roentgen; they suggest wide distribution of such an instrument for general use in the event of disaster.

Everyone who is acquainted with or has worked in the field of protection against undesirable radiations will be in complete agreement with the Lauritsens when they stress the necessity for large-scale use of their instrument or of one of the various protective devices recently developed in other institutions.

Although there are at present numerous articles and books[2] on health monitoring for those exposed to radiations, and these publications describe in great detail all kinds of Geiger counters, ionization survey meters, pocket ionization chambers and film badges, still the average citizen has not been given any satisfactory instruction nor any economical means of making even rough observations regarding the presence of radioactivity, in case of attack.

At present, there is even a shortage of indicating devices in the hands of organized civilian defense authorities. In the event of any kind of attack with radioactive substances, there would be only a small handful of trained persons able to estimate or evaluate the extent of contamination on which to base proper measures of reassurance to the public or orders for evacuation. The burden on these few persons would be so enormous that there almost certainly would be delay in obtaining information in certain localities; such delay might lead to unnecessary fear and even panic, or it might, on the other hand, postpone the necessary treatment for some exposed to dangerous quantities of radiation.

In view of the foregoing, it would seem extremely important that the subject of detection of radioactivity be reduced to its simplest terms and explained to the general public, and that simple, inexpensive means of estimating roughly the quantity of radiation present be available in every home. The instruments developed for detecting and measuring radiations have been refined to such

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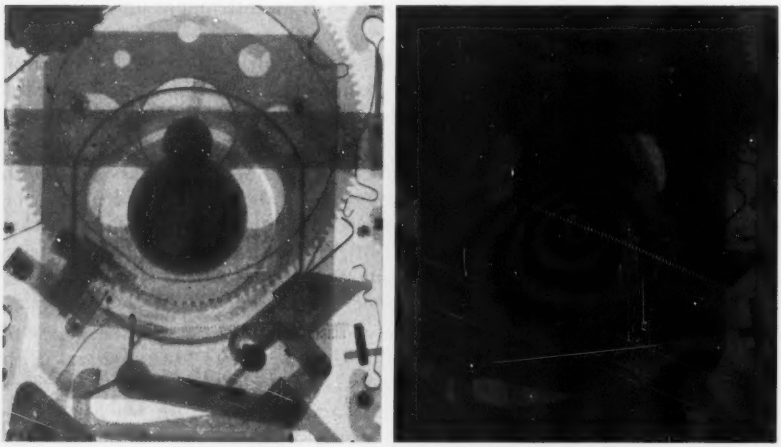
an extent and have become so complex that we sometimes lose sight of the fact that these devices are based on simple principles that can be made understandable to any person of normal intelligence through the use of simple apparatus.

Ever since the discovery of x-rays and of radioactive substances, the principal methods for the detection and measurement of radiations have been based on their effect on photographic film, their effect on fluorescent substances and their ionizing effect on air.[3] These effects constitute the foundation of the whole science of radiology and its practical applications, and the methods based on them are in constant use. The use of x-rays in diagnosis depends entirely on the effect of these radiations on photographic film and the fluorescent screen, and the use of both x-rays and radioactive substances, both natural and artificial, is based on their ionizing effect in tissues.

These three methods, the photographic, the fluorescent and the ionization, or any one of them, may be used in simple ways important in training the average citizen to detect radiations at a nominal cost.



(a) (b)

FIG. 1. (a) Exposure to 4 roentgens (x-ray) of photosensitive paper in the Land Polaroid Camera, with camera shutter closed. (b) Exposure to 1 roentgen (x-ray) of photosensitive paper in the Land Polaroid Camera, with camera shutter closed.

Photographic Method. Every person who has a photographic camera of any kind has a radiation detector in the film. If there is any reason to suspect the presence of ionizing radiation, development of the film would confirm or disprove this. Just at present, this might not be the most practicable method because it would involve some delay while the film is being developed; but research has already been reported[4] on developer solutions which are simple to use and produce speedy results. If a film, after development, is clear, this

would be assuring proof that no radioactivity is present. If the film is gray, this should arouse suspicion of radioactivity, and if the film is dark the presence of a dangerous quantity of radiation is indicated.

The most practicable and rapid photographic method for emergency conditions would be through use of the Land Polaroid camera which includes its own developing system producing a finished picture one minute after exposure. Since with this camera a positive image is obtained direct on the sensitized paper—in contrast to the negative image obtained on ordinary photographic film—the effect of radiation, or the lack of it, is exactly the opposite of that seen on film. That is, if the picture is black, there is no radiation. With a small exposure, the picture is dark, and with a larger exposure to radiation, much lighter. A completely white picture would indicate a large quantity of radioactivity. Figure 1 shows the effect on this polaroid paper of an exposure of 4 roentgens(a) and 1 roentgen(b) (of x-rays), giving a picture of the shutter of the camera. The radiation beam was focused through the shutter, with the shutter closed, for sufficient time to yield the quantities of 4 and 1 r. An exposure of 0.3 roentgen, which is recognized as the maximal permissible dose per week for those working with radioactivity, produces a barely visible outline of the shutter on the dark paper.

The rolls of photosensitive paper used in this type of camera are now available in every photographic and many drug stores. This material could be adapted as a radiation detector without use of the camera. All that would be necessary would be a small box of plastic, wood or metal in which the paper could be pressed flat between the surfaces of the container. If such a device were developed for use in detecting radiations, the sensitive paper probably also could be made available in a flat pack, instead of a roll, which would be more convenient for this purpose. It should be possible also to prepare a chart with which the exposed paper could be compared, to show the lightening effect of various quantities of radiation for different times of exposure.

Fluorescent Method. A simple detection instrument for radiation utilizing the effect on fluorescent materials has been used ever since the discovery of the x-rays. This is a small fluoroscope, such as is illustrated in Figure 2. It can be made easily by anyone inclined to do so, and it could be manufactured in quantity inexpensively. The instrument consists of a tube of metal or other material, open at one end, and closed at the other with a piece of fluorescent screen. (This is manufactured by the Dupont-Patterson Screen Company and may be bought for about 40 cents per square inch.) This end is pointed at the site suspected of radioactivity; if radiations are present, they will cause fluorescence easily visible from the other end in the dark interior of the tube. To enhance the usefulness of this instrument, a small radium-paint button, sold in variety stores for 10 cents, can be fastened in the center of the screen and its light compared with the fluorescent light produced upon the screen by radiation, to get a rough estimate of relative quantity. Small strips of aluminum or copper foil placed on the screen (fig. 2, B and D) permit some estimate of the penetrating power of the radiation being investigated. More elaborate hand fluoroscopes can be obtained from firms handling x-ray equipment.

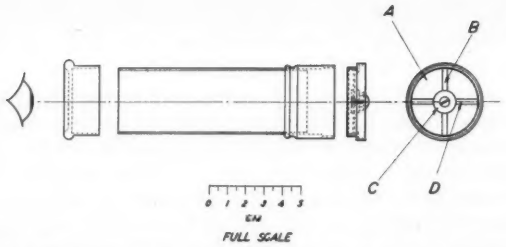


FIG. 2. Diagram of construction of a simple fluoroscope. (A) Fluorescent material (Dupont-Patterson Screen B). (B) Aluminum foil strip. (C) Button with radium-paint. (D) Copper foil strip.

Ionization Method. The instrument recently described by the Lauritsens,[1] like all other ionization instruments, is based upon the principle of the old gold-leaf electroscope. A homemade gold-leaf electroscope can easily be constructed from a bottle or can, a sulfur stopper and a rod carrying a gold leaf (fig. 3), for a total cost of less than a dollar. However, there are also gold-leaf electroscopes on the market which are inexpensive. A simple model is available for $1.35 and one with an improved metal container which can be sealed against moisture for $2.40, from the Central Scientific Company, Chicago. With the addition of a friction rod for charging the instrument, the investment for a rather satisfactory radiation detector is less than $3.00.

Such an instrument could be placed in every home and school room. It would have to be charged every morning or evening, but this would be no more of a burden than the daily winding of a watch or clock. Under normal conditions, the gold leaves would drop or discharge slowly as the result of the weak ionizing effects of natural radioactivity or cosmic radiation. Any quick or sudden discharge would spell danger, for it would indicate ionization from much stronger radiations. This simple electroscope could even be roughly calibrated to indicate the speed of fall of the gold leaves for any dangerous quantity of radiation. This kind of detector would be particularly useful in case of the dispersal of radioactive materials without a bomb explosion.

Comment. Whether we like it or not, it would appear that the atomic age is here to stay, and it is high time that some of the simple facts regarding radioactive substances and ionizing radiations and their effects become known to the average citizen in a way that will enable him to protect himself insofar as possible from the dangers they present. Hitherto, the detection of radiation and its measurement has been the special province of a small group of radiologists and physicists, and so far as the general public is concerned, has been regarded as something in the realm of the unknown and unknowable.

As one who has been closely connected with the handling and study of roentgen rays, radium, radon and artificially radioactive isotopes[5] for 35 years, I am gravely concerned with the present lack of any simple instruction on protection for the average citizen, and with the lack of any kind of indicator

for the detection of radiation that is readily available and practical for use by the unskilled person.

Widespread use of these simple and easily available detectors could perform a useful function in disseminating knowledge of the effects of radiations. Such knowledge on the part of both adults and school children would eliminate some of the aura of mystery and fear that surrounds the whole subject of radioactivity and the menace it presents. This, in turn, should create some feeling of confidence that would help to avert panic in case of disaster.

The simple instruments described herein could be used effectively by science teachers in our schools and colleges to demonstrate the effects of radiation and the principles of protection in a way that is easily understood. The construction of a simple fluoroscope or gold-leaf electroscope might be an impressive feature of such a teaching project. If the average citizen were to devote a few minutes of his radio or television time each evening to a study of the interesting behavior of a simple gold-leaf electroscope, it would be an important step toward understanding the modern physical world in which he lives; it might be also a means of saving himself and his neighbors in case of imminent danger from radioactive substances.

As the knowledge of the individual increases, and as more attention is given to the problem by experts on radioactive protection, the simple apparatus suggested here could always be replaced by better instruments, such as more complex ionization chambers, Geiger counters or scintillation counters, in case such instruments become available in large-scale editions which the average citizen can afford. Actually, the rudimentary devices described would furnish excellent preparation for the handling of more complex and more precise instruments.

It must be recognized, of course, that the simple indicators suggested here would, at best, give only a rough indication of dangerous radiations. But even

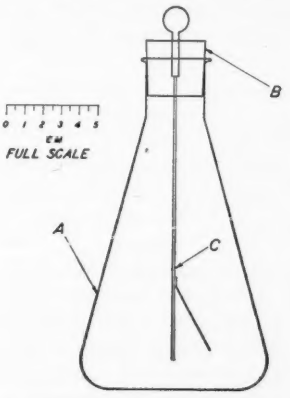


FIG. 3. Simple gold-leaf electroscope. (A) Flask or bottle. (B) Sulfur stopper. (C) Rod with gold leaf.

such a rough indication might mean the difference between life and death under certain circumstances. The details of the effects of various types of radiation upon the photographic plate, the fluorescent screen and the ionizing air volume are manifold and must be carefully studied before any precise evaluation of the reacting meter can be made. These details are amply described in the literature on radiology, and application of this detailed knowledge must remain in the hands of the experts.[5,6]

Nevertheless, in case of widespread disaster either by use of the atomic bomb or the dissemination of radioactive materials, the simple devices suggested herein would give extremely valuable information as to the presence or absence of radioactivity and, to a certain degree, could furnish quantitative data regarding the radiation encountered. A community of citizens instructed in their use would be afforded much more adequate protection in case of sudden danger than is available anywhere at present.

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THE DIAGNOSIS AND SURGICAL TREATMENT OF HYDRONEPHROSIS DUE TO ABERRANT ARTERY

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A VARIETY of lesions may produce upper urinary tract obstruction and if it occurs over a long period of time the back pressure produces a hydronephrosis. The obstruction produced by an aberrant artery is of this type and these cases constitute an interesting group whose symptomatology should be recognized in the differential diagnosis of any pain in the flank or abdomen. Its etiology lies in a congenital failure. The kidney in its embryologic ascent derives its blood supply from successively higher levels as it rises from the pelvis to its final level. As new arteries take over the nutrition of the organ, the previous ones become obliterated until, normally, a single artery remains as the blood supply to the kidney. If one of the previous arteries fails to become obliterated, this one persists and is termed an aberrant artery.

It has been estimated that aberrant vessels are present in 20 per cent of all persons, 80 per cent going to the upper pole of the kidney and 20 per cent to the lower pole. We are not concerned with the former as they are not troublesome, but 80 per cent of all aberrant arteries to the lower pole produces obstruction to the ureter with a resultant hydronephrosis (fig. 1).

Experience with these cases also has shown that these arteries always are associated with fibrous bands which cause the ureter to be closely adherent to the artery; this, I believe, is an important essential to the production of obstruction by creating a fixed point at the ureteropelvic junction. This acts first by impeding normal ureteral peristalsis and secondly by producing angulation of the ureter in the erect posture when the kidney normally tends to drop. A clinical study of these cases leads us to believe that the former mechanism is more important.

That the process is extremely slow and insidious is indicated by the fact that symptoms seldom develop before the age of 15, and a diagnosis is not made in the majority of cases until patients are 20 to 30 years of age. Of 52 patients studied, 30 per cent had symptoms for 10 or more years and 55 per cent for at least 3 years before a diagnosis was made. This indicates that the condition is frequently unrecognized. Nine patients had had previous abdominal operations without relief of symptoms.

The condition is more commonly unilateral, but may involve both kidneys, a fact which must be remembered when considering operation.

Diagnosis: In the diagnosis of this lesion, the case history is important. A person in the second or third decade of life may complain of pain in the flank or abdomen. In most instances it is a periodic type of pain which may appear suddenly, become intense though seldom colicky, then gradually subside over a period of from one to several days. At the height of the attack,

reflex nausea and vomiting may be severe and may lead frequently to an erroneous diagnosis of an intraperitoneal lesion. In the presence of infection the attack may be initiated by a chill and fever. In other cases the pain may be continuous, dull, aching and boring, which type is more likely to occur in the late stages. In many cases the pain is most severe on arising and gradually subsides after the patient becomes active. This fact corroborates the previous assumption that interference with ureteral peristalsis is a more important factor in production of the hydronephrosis than the dropping of the kidney in the upright posture. The cessation of pain on resuming muscular activity after a night's rest probably can be attributed to a squeezing effect on the dilated pelvis which gradually expresses the urine that has accumulated during the night.

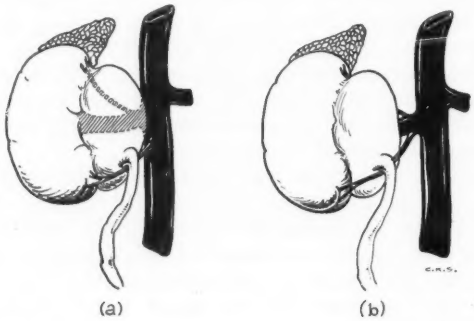

FIG. 1. Diagrammatic drawing showing manner in which the anomalous vessel produces ureteropelvic obstruction. (a) This vessel may be a branch of the aorta or (b) a branch of the renal artery.

Physical signs may not be striking. There is usually some tenderness in the costovertebral angle of the affected side which may be elicited only by first percussion. In rare instances, there may be a palpable mass in the kidney region. As many of these kidney pelves are uninfected, there may be negative urine which too often results in exoneration of the urinary tract. The urinalysis, therefore, is not a reliable indication in the diagnosis. It is significant that in 50 per cent of our cases the urine was entirely normal.

The **diagnosis** can be arrived at only by making a pyelogram either by intravenous urography or retrograde pyelography after ureteral catheterization. If the former method is employed one must remember that kidney function may be impaired resulting in a delayed appearance of the dye in the renal pelvis. If the condition is suspected delayed films made 2 or even 3 hours after injection of the dye may demonstrate a hydronephrosis. Kidney function may be destroyed so completely that no visualization will occur. The characteristic picture in the moderately advanced case is a kettle drum type of hydronephrosis in an extrarenal pelvis. The opaque medium is sharply confined to

the pelvis and there seldom is any dye in the upper ureter, thus indicating the obstruction to be at the ureteropelvic junction. In the retrograde pyelogram one usually sees a high insertion of the ureter and often the angulation is such as to prevent the ureteral catheter from entering the renal pelvis (fig. 2).

All patients with hydronephrosis associated with ureteropelvic obstruction should be hospitalized for retrograde pyelography. Because of the stasis in the kidney, acute infection may complicate the procedure in spite of most careful precautions. The patient may become severely ill and require immediate surgical intervention.

The **treatment** is by surgical methods which may be conservative in an attempt to save the kidney, or radical such as nephrectomy in those cases in which the process has resulted in complete destruction of the kidney. The operation, therefore, is dependent upon the extent of kidney damage, which in turn is related to the duration of the disease. In our cases, the average duration of symptoms where nephrectomy was required was 7.2 years, as opposed to 4.1 years when conservative measures were employed. Thus the importance of early diagnosis is apparent.

Determinations of the kidney function are required to ascertain the degree of damage. If the kidney shows absence of function and the pyelogram reveals the large type of hydronephrosis, nephrectomy is indicated. When the function is diminished in a young person whose symptoms are of relatively short duration, a more conservative operation should be selected to save the kidney.

Various types of conservative operations have been advocated, the chief controversy revolving about the advisability of ligating the obstructive artery. Those who oppose this procedure call attention to the fact that the arteries to the kidney are so-called "end" arteries and that a division results in necrosis of the portion of the kidney supplied by that vessel. To save the artery, various plastic procedures have been devised involving two principles: (1) to draw the ureter away from the artery and (2) to divide the ureter and reimplant it into the kidney pelvis on the opposite side of the obstructing vessel. Good results have been reported by both methods.

Our experience, however, is that no ill effects follow ligation of the artery. The operation consists of exposing the ureter and renal pelvis through the usual incision, and demonstrating the obstructing artery. The latter is isolated and the portion lying over the ureter excised. Subsequently it is extremely important to completely free the ureter of all fibrous periureteral bands. Following this procedure the ureter usually affords good dependent drainage of the renal pelvis. It is advisable to pass a 12 or 14 F catheter from the pelvis into the ureter to exclude the possibility of concomitant ureteropelvic stricture.

The foregoing procedure was used in 21 of the 52 cases studied and the results have been uniformly good. Pain has been relieved in every case and, in most instances, there has been prompt improvement in kidney function and reduction in size of the hydronephrosis. The reduction may be a slow process and, in many cases, the pelvis never returns to an absolutely normal size; however this is unimportant if pain has been relieved and if the kidney functions

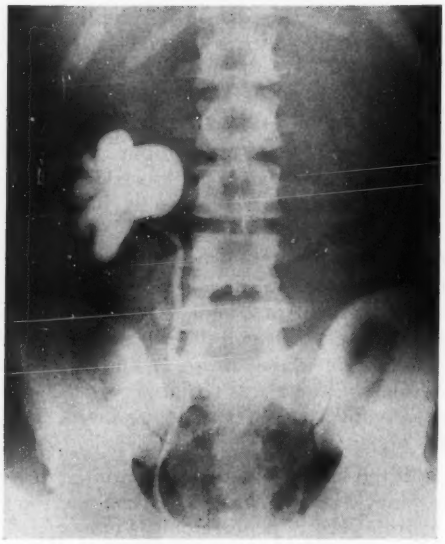

FIG. 2. Retrograde pyelogram showing hydronephrosis and angulation of ureter associated with ureteropelvic obstruction due to an aberrant artery.

satisfactorily. Such a kidney is capable of sustaining life in the event that the opposite kidney becomes impaired.

Summary

This experience indicates that ligation of an obstructing aberrant artery to the lower pole of the kidney is a safe and logical procedure in relieving this type of ureteropelvic obstruction. If there is subsequent destruction of kidney tissue, it is reflected neither in the convalescence nor end results obtained by the patient. It presents more promise in the average case than the more complicated plastic procedures which have been advocated because it avoids the opening and extensive handling of the renal pelvis, and does not interfere with the normal neuromuscular mechanism. Moreover, it minimizes the possibility of postoperative kidney infection which is the most frequent cause of failure in conservative surgery of the kidney.

LYMPHATIC LEUKEMIA OCCURRING SIMULTANEOUSLY IN NEGRO BROTHER AND SISTER

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THIS report concerns a brother and sister, Negroes, a year apart in age, who apparently developed chronic lymphatic leukemia simultaneously. It is of special interest because: (1) we have found no report in the literature of instances of leukemia developing in members of the same family at so nearly the same time and age; (2) it is unusual for members of the same family to develop leukemia; (3) the occurrence of leukemia in the Negro race is less frequent than in the Caucasian, according to the report of Pizzolato[1] who reviewed a series of cases of leukemia at Charity Hospital, New Orleans, where a high percentage of patients are Negroes.

Case Reports

Case 1. A man, aged 40, was admitted to the Cleveland Clinic on February 22, 1946, complaining of swellings about the neck which had increased in size during the previous 9 months. The swellings interfered with breathing and swallowing and caused choking sensations. The patient also had been aware of lumps in his right armpit for the past month. His previous illnesses were noncontributory.

Pertinent physical findings included large, discrete, elastic nontender masses of enlarged nodes which were palpable in each side of the neck, in each axilla and in the groins. His tonsils completely obliterated the otopharynx; the spleen was enlarged to 10 cm. below the left costal margin. Roentgenograms showed enlargement of mediastinal nodes.

Laboratory examinations were normal except for the blood findings. The red cell count was 5,100,000 with slight anisocytosis, poikilocytosis and pallor. Nucleated red cells, 1/100; hemoglobin 13.5 Gm. per 100 cc. (88 per cent); color index 0.85. The white cell count was 110,500; neutrophils 20 per cent, lymphocytes 72 per cent; monocytes and platelets were decreased. A diagnosis of chronic lymphatic leukemia was made.

Roentgen therapy was instituted and given periodically to the neck, both groins and axillae, and to the mediastinum and epigastrium, depending upon the patient's general condition, size of lymph nodes, and blood counts. Improvement continued for about a year after which he failed rapidly. The white cell count ranged from 6000 to 45,000 while the red cells and hemoglobin were fairly normal. As the patient's condition became worse the white count rose to 140,000 with almost 100 per cent lymphocytes, 1,050,000 red cells and hemoglobin 25 per cent. Transfusions of whole blood were given. However the patient died in February 1948, 2 years after admission to the Clinic.

Case 2. The sister of the patient in the previous report was admitted to the Clinic 1 month later. The 41-year-old Negress complained of swelling in the neck, axillae, groins, and "a bad tumor" in the stomach. She had been taking penicillin for "bad blood" and skin trouble.

On observation generalized lymphadenopathy was found to be present, the spleen was enlarged to the pelvic brim, and the liver was enlarged also. A mass in the pelvis was presumed to be a fibroid tumor.

The patient's red cell count was 2,300,000 with moderate anisocytosis, and poikilocytosis (1/100 white blood count in nucleated forms). Hemoglobin was 30 per cent. White blood count was 553,000 with 97 per cent lymphocytes, some representing early forms. Platelets were decreased. Wassermann test was 3 plus. A diagnosis of chronic lymphatic leukemia was made.

Roentgen therapy was given periodically to the neck, axillae, groins, epigastrium, pelvis and spleen. The white blood count dropped to 5800 in 2 months and the patient felt much improved. Whole blood transfusions were given also.

In December 1946 she developed generalized vesicular dermatitis. Mucous membranes were pale and petechial hemorrhages were present in the mouth. This condition was diagnosed as generalized herpes zoster, frequently observed in chronic leukemia.

The patient gradually became worse and on September 9, 1947, the white blood cell count rose to 245,000. She died shortly thereafter.

Comment

The familial incidence of leukemia presents an interesting problem. The most comprehensive review on the subject was given by Ardashnikov[2] in 1937. He found that 31 instances of leukemia occurring in 2 members of the same families had been reported. He concluded that in some cases, at least, hereditary factors play a role in the etiology of leukemia.

Hornbaker[3] reported cases of chronic leukemia in 3 sisters in 1942. He believes that there is no sufficient evidence to explain the occurrence of familial leukemia on the basis of heredity, except for the known hereditary factor in malignant diseases among which leukemia is now generally classified.

Frech[4] reported cases of chronic leukemia occurring almost simultaneously in brothers. Sturgis[5] presented a case of subleukemic myelogenous leukemia in a 37-year-old man whose sister had died of subacute histiomonocytic leukemia 1 month previously. He believes that the occurrence of more than one case of a rare disease in a blood relative is due to chance.

We do not believe there is sufficient evidence to indicate that hereditary factors play an important role in leukemia. Our 2 cases probably were adventitious.

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CUTANEOUS SENSITIVITY TO MONOGLYCEROL PARA-AMINOBENZOATE

Cross Sensitization and Bilateral Eczematization

Report of a Second Case

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PARA-AMINOBENZOIC acid, hereinafter referred to as PABA, and its metallic salts are used in the treatment of such diseases as lupus erythematosus, dermatomyositis, the rickettsial diseases, dermatitis herpetiformis, scrub and murine typhus fevers, rheumatic fever, leukemia and vitiligo. Many of the local anesthetics such as procaine, monocaine, pontocaine and butyn are derivatives of PABA as well as certain of the so-called skin analgesics including benzocaine and butesin.

Rothman and Rubin[1] recently discussed the sunburn preventive effect of PABA, incorporated in ointment bases and lotions. As a result of this preventative action, certain of the alkyl and alcoholic agents derived from PABA are the principal constituents of commercial lotions. We know of two such preparations, one of which contains monoglycerol para-aminobenzoate and the other propylene glycol para-aminobenzoate. There is evidence that internal organs, the liver and hematopoietic system, may become sensitized to PABA. Systematic reactions and eczematous contact-type dermatitis are well known phenomena produced by local anesthetics and skin analgesics. Dyes, such as the azo variety, paraphenylenediamine, and aniline frequently sensitize the skin as do the sulfonamides. These two groups of compounds are closely related to PABA and its derivatives in molecular structure because of the common aminobenzene nucleus ($H_2N\ C_6H_5$) and the often structurally allied side chains. The similarity in molecular structure may be said to be the basis for cross sensitization.

Clinically, this cross sensitization has been extensively studied in contact dermatitis. Sulzberger et al[2] observed positive reactions to patch tests with PABA in persons who showed cross reactions among the sulfonamides. Fascinating studies of cross sensitivity in dermatitis caused by local anesthetics (PABA derivatives) which extended even to anesthetics not structurally related, have been reported by Rothman et al,[3] Goodman,[4] Strauss,[5] James[6] Laden and Wallace,[7] Laden and Rubin[8] and others. A thought provoking study was made by Baer et al[9] who suggested that in cross sensitization between azo dyes incorporated in foods and paraphenylenediamine (a constituent of hair and clothing dyes), cross-eczematous dermatitis is possible. Lever's and Luikart's[10] patient who evidenced positive reactions to patch tests with dyes, local anesthetics (PABA derivatives), PABA and its alkyl ester derivatives

(surface anesthetics), also had an eczematous dermatitis medicamentosa caused by PABA.

Meltzer and Baer[11] first reported eczematous dermatitis caused by monoglycerol para-aminobenzoate in a patient who had applied a commercial sunburn preventive. They found a wide range of cross sensitivity to para-aminobenzoic acid, its local anesthetic and skin analgesic derivatives, sulfonamides, and structurally related dyes, as well as other anesthetics and chemicals not thus related. We report herein a second case of sensitization to monoglycerol para-aminobenzoate in which cross sensitivity was demonstrated to the alkyl ester derivatives (butesin, benzocaine), paraphenylenediamine and aniline, but with an additional observation that the eczematous dermatitis was reproduced in the patient by ingestion of para-aminobenzoic acid.

Case Report

A white woman aged 40, housewife and part time cashier, was admitted to the Cleveland Clinic December 21, 1948. She complained of an itching eruption readily identified as lichen ruber planus, and which followed a "sunburn." The patient also presented a localized area of eczematoid dermatitis on the left foot of 2 months' duration which had occurred on the same site 7 years previously. A year prior to admittance, she had experienced an attack of acute urticaria which had developed at the end of 4 days' administration of a sulfonamide, probably sulfadiazine.

The lichen planus has been persistent with the exception of a remission of about 2 months' duration. During the remission the patient applied a sunburn preventative to her husband's skin and within 4 hours she developed itching, and within 24 hours, an acute vesicular and edematous dermatitis appeared on the hands, and patches on the forearms, arms, face and neck. At this time, it became known that the same lotion had been applied to her skin when she acquired the "sunburn" in July, 1948. The dermatitis rapidly subsided following treatment with soothing wet dressings and lotions. Three months later, she took a 100 mg. dose of para-aminobenzoic acid followed the next day by an erythema with itching on the hands and forearms. The dorsa of the hands were slightly swollen but there was no vesiculation. The reaction subsided during the next 3 or 4 days.

The manufacturer obligingly supplied the various ingredients of the suntan lotion in suitable form for patch tests. Other significant chemicals also were applied to the patient's skin as patch tests in standard concentrations. The patches were removed at the end of 48 hours and observed again at the end of 72 hours. The results are recorded in Table 1. For the sake of brevity, test number 1 which is recorded as negative, represents the negative results of 6 patch tests with combinations of the various ingredients of the lotion.

Comment

The sunburn experienced by our patient may have been the trigger mechanism for the development of lichen planus. Not infrequently a history of chronic nervous exhaustion, mental strain or shock, or trauma precedes the onset.

For some years the patient had been under the strain of two jobs and symptoms of an anxiety state were manifest; hence the subsequent development of lichen planus was not considered unusual.

Table 1

COMPARISON OF RESULTS OF PATCH TESTS WITH INGREDIENTS OF A SUNBURN PREVENTIVE LOTION AND STRUCTURALLY RELATED AND NONRELATED COMPOUNDS

Chemicals Tested	Meltzer's and Baer's[11] Patient	Our Patient
1. Various ingredients of sunburn preventive lotion other than monoglycerol PAB*	0	0
2. Monoglycerol PAB*	4+	4+
3. PABA	4+	4+
4. Benzocaine	4+	4+
5. Butesin	4+	-----
6. Butyn	-----	4+
7. Procaine	4+	0
8. Pontocaine	0	0
9. Sulfaquanidine	3+	0
10. Sulfanilamide	3+	0
11. Sulfadiazine	1+	0
12. Sulfathiazole	-----	0
13. Aniline	4+	2+
14. Paraphenylendiamine	4+	3+
15. Azo dye "A"	2+	-----
16. Azo dye "B"	0	-----
17. Nupercaine	1+	0
18. Saccharin	2+	0
19. Picric acid	3+	0
20. Metycaine	-----	0
21. Stovaine	0	-----
22. Paranitrobenzoic acid	0	0
23. Phenol	0	0
24. 3 5 Dinitrobenzoic acid	0	-----
25. Anthranilic acid	0	-----
26. Apothesine	0	-----
27. Methyl anthranilate	0	-----
28. Alypin	0	-----
29. Paranitrobenzaldehyde	-----	0

*Supplied by the manufacturer.

Of considerable interest was the sensitization to monoglycerol PAB and the demonstration of cross sensitivity to related chemicals. Our case may be compared to that of Meltzer and Baer which showed a much wider range of cross sensitization (table 1). Among factors influencing sensitization in eczematous dermatitis are the capacity of a chemical compound to sensitize, frequency of exposure, unilateral or bilateral transepidermal penetration, and the physical conditions at the skin surface. It is not known what possible decomposition products form a breakdown of a chemical, or what chemical protein conjugates (hapten linkage), producing an eczematous dermatitis, are formed

on or within the epidermis. Explanations for cross sensitivity have been based on analysis of the molecular structural relationships between primary and secondary allergens e.g. the nucleus, substituted radicals in the nuclei, and/or the whole or portions of the side chains. Experiments utilizing the patch test with compounds closely approximating the various parts of the molecule of the primary eczematizing chemical have partially substantiated this hypothesis. Baer[12] assumes that the sensitized cell may be unable to differentiate between a primary allergen, and/or its conversion products or the secondary allergen. However, this hardly explains the limited range of cross sensitization even among members of a homologous group of compounds as well as the broader spectrum of cross sensitivity including apparent heterologous chemicals.

The immunochemical theory of complementariness for the precipitin reaction discussed by Pauling, Campbell and Pressman[13] may conceivably account for cross sensitization by the interaction of the hapten-protein group formed from sensitizing compounds in the epidermis and the cellular proteins (antibodies?). The haptenic groups assume molecular spatial relationships which provide certain corresponding surface areas for the forces such as Van der Wool's attraction, hydrogen bond formation, and interaction of electrically charged groups to attract. The complementary antibody polypeptid chains then fold into a stable configuration in the presence of the antigen, and the reaction takes place. Thus for every antigen (allergen) a specific complementary antibody is present.

We may postulate that a sensitizing compound on entering the skin may form one or more different haptenic groups or, assuming a breakdown of the chemical in the body or epidermis, the products may form one or more hapten-protein groups. Formation of cellular antibodies may result to only a few or perhaps to many of the groups. In a person having had multiple or polyvalent episodes of eczematous dermatitis to different chemicals, the number of haptenic groups and corresponding antibodies may be greatly multiplied. Conversely, one episode of eczematous dermatitis to only one compound may result in the formation of a relatively few antigens. Applying the complementariness theory, a smaller or larger number of the antibody polypeptid chains within the cell may fold into a spatial configuration stable in the presence of the haptenic groups. We believe that the immunochemical theory of complementariness may explain why Meltzer's and Baer's patient who had several episodes of contact type eczematous dermatitis to different chemicals showed cross reactions to 14 compounds and our patient, having a single outbreak of eczematous dermatitis to but one chemical, evidenced positive reaction to only 6 closely related compounds.

In the cases studied by the authors herein referred to, 85 chemicals were applied by the patch test technic. The majority of the patients were physicians and dentists who handled local anesthetics. In Table 2 we have collected those chemicals producing positive reactions into groups and in the order of frequency of administration. If one wishes to determine the trend of cross sensitivity in a patient who is sensitive to a probable local anesthetic, one may select

Table 2

FREQUENCY OF POSITIVE PATCH TESTS IN 22 PATIENTS PRESENTING CROSS SENSITIZATION REACTIONS

Name	Molecular Formula	Number of Patients with Positive Reactions
I. Local anesthetics. Esters of PABA with a tertiary amine in the side chain		
Procaine	$H_2N \cdot C_6H_4 \cdot CO_2 \cdot C_2H_4 \cdot N : (C_2H_5)_2$	18
Monocaine	$H_2N \cdot C_6H_4 \cdot CO_2 \cdot C_2H_4 \cdot NH \cdot CH_2 \cdot CH : (CH_3)_2$	10
Larocaine	$H_2N \cdot C_6H_4 \cdot CO_2 \cdot C(CH_2)_2 \cdot CH_2 \cdot N : (C_2H_5)_2$	10
Tutocaine	$H_2N \cdot C_6H_4 \cdot CO_2 \cdot CH(CH_3) \cdot CH(CH_3) \cdot CH_2 \cdot N : (CH_3)_2$	9
Butyn	$H_2N \cdot C_6H_4 \cdot C_3H_6 \cdot N : (C_4H_9)_2$	8
Pontocaine	$C_4H_9 : N \cdot C_6H_4 \cdot CO_2 \cdot C_2H_4 \cdot N : (CH_3)_2$	5
Procaine borat	$H_2N \cdot C_6H_4 \cdot CO_2 \cdot C_2H_4 \cdot N : (5\,HBO_2)\,(C_2H_5)_2$	3
II. Surface anesthetics. Alkyl esters of PABA and substituted compounds		
Benzocaine	$H_2N \cdot C_6H_4 \cdot CO_2 \cdot C_2H_5$	6
Butesin	$H_2N \cdot C_6H_4 \cdot CO_2 \cdot C_4H_9$	4
Orthoform	$H_2N \cdot C_6H_3(OH) \cdot CO_2 \cdot CH_3$	1
Neo-orthoform	$OH \cdot C_6H_3(NH_2) \cdot CO_2 \cdot CH_3$	1
III. Sunburn preventives, PABA, alkyl esters of PABA and metallic salts of PABA		
PABA	$H_2N \cdot C_6H_4 \cdot CO\,OH$	7
Sodium PAB	$H_2N \cdot C_6H_4 \cdot C\,O\,O\,Na$	2
Monoglycerol para-aminobenzoate	$H_2N \cdot C_6H_4 \cdot CO_2 \cdot CH_2 \cdot C\,H\,O\,H \cdot CH_2O\,H$	2
IV. Chemotherapeutic agents. Sulfanilic acid derivatives structurally related to PABA		
Sulfadiazine	$H_2N \cdot C_6H_4 \cdot SO_2 \cdot N : C_4N_2H_3$	5
Sulfanilamide	$H_2N \cdot C_6H_4 \cdot SO_2 \cdot N\,H_2$	4
Sulfaquanidine	$H_2N \cdot C_6H_4 \cdot SO_2N : C : (NH_2)_2$	3
Sulfathiazole	$H_2N \cdot C_6H \cdot SO_2 \cdot N\,H \cdot S \cdot N \cdot C_3H_2$	2
V. Dyes		
Aniline	$H_2N \cdot C_6H_4$	4
Paraphenylene-diamine	$H_2N \cdot C_6H_4 \cdot NH_2$	4
Azo dye "A"	$CH_3CO \cdot HN \cdot C_6H_4N : N \cdot C_6H_3OH\,Cl$	1
Methyl orange	$(CH_3)_2N \cdot C_6H_4N : N \cdot C_6H_4SO_2OH$	1
VI. Miscellaneous. Includes local anesthetics and compounds that may or may not be structurally related to PABA		
Para-aminophenol	$H_2N \cdot C_6H_4OH$	3
Apothesine	$C_6H_5 \cdot CH : CH \cdot CO_2 \cdot C_3H_6 \cdot N : (C_2H_5)_2$	2
Alypin	$C_6H_5CO_2 \cdot C : [\cdot CH \cdot N(CH_3)_2]\,[\cdot CH_2 \cdot N(CH_3)_2]\,C_2H_5$	1

one or more chemicals from the several groups for preliminary patch tests. On the other hand we agree with Sulzberger and Baer[14] that the important motive, from the patient's standpoint, is to determine the chemicals which may be considered "safe" as determined by negative patch tests. In the patient sensitive to a local anesthetic, positive patch tests would more likely be obtained with chemicals of the same group than with other chemicals. Conversely, negative reactions are more frequently obtained with local anesthetics or other chemicals not listed in the groups in Table 2.

An eczematous reaction was reproduced in one of Lever's and Luikart's patients, and in our own, by ingestion of small amounts of PABA. It is recognized that some chemicals may, by transepidermal penetration either from within or without the body or both, cause an eczematous dermatitis. Baer, Leider and Mayer[9] have indicated the possible dangers of cross sensitization reactions between dyes in foods and dyes in clothing or those having come in contact otherwise with the skin. Cross sensitization induced by para-aminobenzoic acid, (presumably a factor in the vitamin B complex) and/or its derivatives, and structurally related compounds by virtue of their wide use in medication, in foods, and in contactants may be a potential factor in eczematoid dermatitis of unknown origin.

Summary

A second case of cutaneous sensitivity to monoglycerol para-aminobenzoate, an ingredient of a proprietary sunburn preventative, is reported. The dermatitis was reproduced by ingestion of para-aminobenzoic acid. Cross sensitivity to PABA, certain of its alkyl derivatives, and structurally related dyes was demonstrated. The immunochemical theory of complementariness between allergen and cellular antibodies in the epidermis is discussed in relation to cross sensitization in the skin. A compilation of chemicals is arranged in groups and in order of frequency in producing positive reactions from which structurally related chemicals may be selected for a rapid survey by the patch test technic in order to determine the trend of cross sensitization.

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TREATMENT OF PHARYNGO-ESOPHAGEAL DIVERTICULUM BY INVERSION OF THE SAC*

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IN 1895 Girard[1] of France first reported treatment of pharyngo esophageal diverticulum by simple inversion. Subsequently Halstead[2] and Bevan[3] independently utilized the procedure and reported its success. Since that time, except for an occasional report such as that made by Ross,[4] the technic has not been described in the literature and generally has been replaced by the technics of excision of the diverticulum as reviewed by Lahey,[5] Harrington,[6] and others.

A pharyngo-esophageal diverticulum is composed of mucosa and submucosa herniating through the zone of the junction of the pharynx and esophagus and through the triangular space bounded by the fibers of the cricopharyngeal muscle and the inferior constrictor of the pharynx. The position of the sac may be in the midline or usually to the left between the two muscles (fig. 1). The structure and relationship of the sac renders it possible to reduce the herniation by inversion of the sac and closure of the muscular defect. This procedure has been performed in a series of 11 consecutive cases of pharyngo-esophageal diverticula by the following technic:

Technic

1. Unless the roentgenographic investigation demonstrates clearly that the diverticulum originates on the right side (which is rare) an incision is made through skin and platysma over the anterior edge of the left sternocleidomastoid muscle from the level of the hyoid bone to the suprasternal notch.

2. The sternocleidomastoid and prethyroid muscles are retracted laterally and the lobe of the thyroid medially. To provide adequate exposure, it usually is necessary to ligate and divide the lateral thyroid vein and inferior thyroid artery.

3. The recurrent laryngeal nerve is identified and its upper portion clearly exposed so that inadvertent injury of the nerve will be avoided.

4. The diverticulum is identified lying directly behind the lobe of the thyroid and is carefully grasped with smooth thumb forceps. The sac is dissected away from the muscle fibers of the inferior constrictor and cricopharyngeus muscles until its neck is well mobilized.

5. An Ewald tube is passed by the anesthetist through the mouth and down the esophagus to outline the esophagus and aid in identifying the true neck of the sac.

6. A purse string suture of catgut is placed through the submucosa of the neck of the sac and the sac is inverted into the esophagus (fig. 2a).

7. The purse string suture then is tied and the Ewald tube passed through again to demonstrate the absence of esophageal stricture (fig. 2b).

8. With the Ewald tube resting in the esophagus and the sac inverted, the defect between the muscle fibers of the cricopharyngeus and inferior constrictor muscles is closed transversely with interrupted Number 60 cotton sutures.

9. The subplatysmal structures of the neck are allowed to fall together, platysma and fascia are closed without drainage with Number 60 cotton sutures, and skin edges are approximated with clips.

10. The Ewald tube is withdrawn.

Postoperative Care

The patient is allowed to be ambulatory on the day of operation, permitted clear liquids for the first 2 postoperative days, and on the third day a soft diet is given. Skin clips are removed on the third or fourth postoperative day, and the patient is discharged on the fifth to seventh day on an unrestricted diet with instructions to chew his food thoroughly.

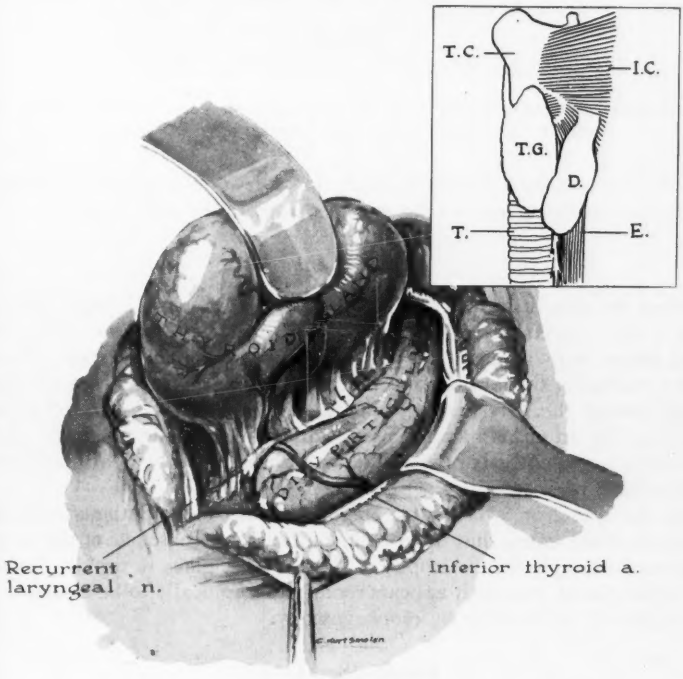


FIG. 1 inset. T.C. (thyroid cartilage), I.C. (inferior constrictor muscle), T.G. (thyroid gland), D. (diverticulum), T. (trachea), E. (esophagus).

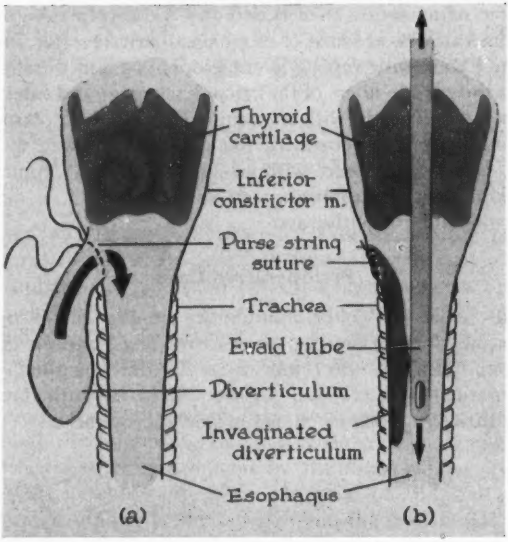


FIG. 2. (a) Diverticulum mobilized; purse-string suture in place. (b) Diverticulum inverted; purse-string suture tied; Ewald tube in esophagus.

Penicillin was used prophylactically for a few postoperative days in the first patients in the series, but has not been used in the later cases.

Comment

When the diverticulum is exceptionally large (as in case 3 which measured 11 by 7 cm.), inversion is dangerous without partial resection. If the entire diverticulum were inverted the patient might belch it into the pharynx, thereby occluding the larynx. In order to avoid this contingency a tie may be placed around the diverticulum and its distal two-thirds resected prior to inversion. The stump is handled aseptically, but since the possibility of contamination is present it is best to insert a Penrose drain which should be left in place for 2 or 3 days.

For the first 2 or 3 days after operation some of the patients with larger diverticula have stated that upon belching, they are conscious of the presence of the sac in the pharynx. Atrophy of the sac takes place so rapidly, however, that at the end of 2 weeks it appears roentgenographically to be a small polyp, and is difficult to visualize by esophagoscopy.

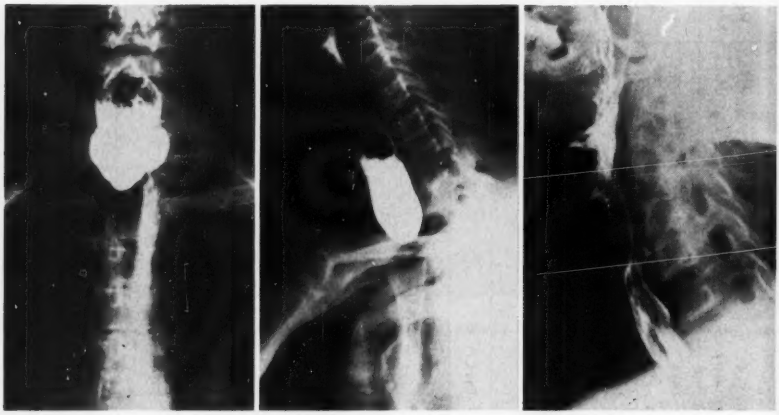
Results (See Table)

The 11 patients treated by the technic described, have done well. In a single case a second small bulge appeared on the opposite side, but has not caused

Case No. *	Size of Diverticulum (X-ray Measurement)	Restricted Diet	Postop. Complication	Postop. Day of Discharge	Postop. X-ray	Postop. Esoph.	Follow-up Mo. Postop.	Results
1	5.5 x 9 cm.	1 week	0	6 days	No recurrence	No diverticulum	2 mo. **	Cured
2	3.5 cm.	4 days	0	5 days	No recurrence	.....	48 mo.	Cured
3	11 x 7 cm. left post. wall	4 days	0	5 days	Small diverticulum, rt. post. wall	.....	20 mo.	Cured—Small new diverticulum, on other side
4	Large	6 days	0	6 days	.....	.....	38 mo.	Cured
5	4 x 2 x 4.5 cm.	4 days	0	7 days	Small filling defect at site of diverticulum, no recurrence	.....	24 mo.	Cured
6	3.5 x 2.5 cm.	6 days	0	8 days	No recurrence	No diverticulum	24 mo.	Cured
7	4 x 5 cm.	3 days	0	3 days	.....	.....	14 mo.	Cured
8	3 x 2 x 3 cm.	5 days	0	5 days	.....	.....	17 mo.	Cured
9	4 cm.	5 days	0	7 days	Small filling defect at site of diverticulum	.....	19 mo.	Cured
10	3 x 6 cm.	5 days	0	10 days	No recurrence	.....	20 mo.	Cured
11	.....	4 days	Infection requiring drainage	4 days	No recurrence	.....	15 mo.	Cured

*Five of these patients were operated upon by the late Dr. T. E. Jones.
**Unable to trace.

symptoms of sufficient significance to require treatment. The patients have been followed from 2 to 38 months since operation and there have been no recurrences, strictures, or late complications (fig. 3). In one case a patient who had had an uneventful postoperative course in the hospital, and who was discharged on the fourth postoperative day, developed a deep cellulitis of the neck several days afterwards. The cellulitis responded to treatment with antibiotics but ultimately required drainage. There was no fistula and there has been no recurrence of the diverticulum.



(a) (b) (c)

FIG. 3. (a and b) Case 1. Preoperative x-rays revealing large pharyngo-esophageal diverticulum. (c) Postoperative x-ray. No evidence of recurrence.

Advantages

1. The esophagus is not opened, so that danger of infection is minimized.
2. The period of hospitalization has been shortened so that the majority of patients are ready for discharge on the fourth or fifth postoperative day.
3. There is no necessity for tube feeding.
4. Liquids are given from the time of operation and a normal unrestricted diet can be resumed on the fourth postoperative day.
5. The incidence of recurrence is low because of the absence of infection.

Conclusions

1. A technic of repairing pharyngo-esophageal diverticula by inversion of the sac and repair of the overlying musculature is described.
2. The operation is simple, safe, and aseptic.
3. The end results in our 11 cases have been entirely satisfactory.

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CHRONIC BERYLLIUM POISONING

(Chronic Pulmonary Granulomatosis)

Preliminary Reports on Four Cases Treated with ACTH

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THE following case reports add confirmation to the recent article by Kennedy et al[1] (2 cases) which states that subjective and objective improvement have been demonstrated by the administration of ACTH in instances of chronic beryllium poisoning. Heretofore no therapy affording even temporary improvement has been found by us in progressive and severe cases of this disease. The factor of exposure to beryllium and/or its compounds has been present in each instance.

Case Reports

Case 1. A white man now 50 years of age was employed in a beryllium basic production plant on April 30, 1945. For the first 7 days he worked with the soluble fluoric salt compounds of beryllium but was transferred, because of evidence of dermal intolerance, to a department where melted and ground ore was treated with sulfuric acid. Three weeks later he developed a spasmodic productive cough, substernal discomfort and exertional dyspnea. A clinical diagnosis of acute chemical bronchitis was established. Roentgen examination of the chest was negative. Under ambulatory symptomatic therapy he made an uneventful recovery and returned to work on July 9, 1945; however, within 10 days the patient had a recurrence of subjective and objective symptoms. Following complete recovery he was ordered medically released from the industry on September 11, 1945.

His subsequent place of employment was approximately one and one-half miles from the beryllium plant and his permanent residence about nine miles away.

In October 1947 he first became aware of a refractive spasmodic productive cough, a progressive exertional dyspnea, and anorexia with associated weight loss.

The paroxysmal cough gradually increased in intensity and frequency and the expectorated mucus developed a greenish tinge. Exertional dyspnea and anorexia became pronounced. Eventually the severity of the symptoms forced him to forego all physical work in March 1948.

During the first 2 years of the disease the coughing paroxysms were associated with vertigo. Frequent attacks of "mild chills" and fever were experienced during the

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first few months following the onset and to a lesser degree up to the time of hospitalization in August 1950.

The patient was referred for consultation on April 26, 1948 following interpretation of a pulmonary roentgenogram. Temperature was normal, pulse 75, and respiratory rate 20. Blood pressure was 95/70. The vital capacity was read at 3.4 L. and computed as 82 per cent of the expected normal. The breath holding time was 20 seconds.

The patient did not appear acutely ill. Respiratory distress was not apparent at rest nor was acrocyanosis present.

Equal thoracic limitation of motion was noted on forced inspiratory effort at which time the patient complained of substernal pain. Percussion tone was unimpaired. No abnormalities were detected on auscultation.

The pulmonary roentgenogram taken on April 13, 1948 revealed a diffuse, granular involvement throughout the parenchyma of both lung fields. There was an associated prominence of hilar shadows without nodulation. X-rays of the hands showed no osseous changes. Clinical studies on blood and urine were essentially normal at this time. A diagnosis of "chronic pulmonary granulomatosis in a beryllium worker" was made.

The patient has been examined at regular and frequent intervals for the progress of the disease. Specialized studies were conducted at Rochester University School of Medicine in the fall of 1948.

Despite varied and intensive supportive therapy since the initial examination the patient became progressively worse and consequently was hospitalized on August 15, 1950.

Examination on hospital admission revealed a severely emaciated, mentally depressed patient exhibiting dyspnea at rest. Spasmodic coughing was pronounced during the entire examination.

Blood pressure was 110/74. The weight was 120, a 60 pound loss since the onset of symptoms in 1947. The vital capacity was read at 2.0 L. and computed as 48 per cent of the expected normal. Acrocyanosis and early clubbing of the finger tips were noticed. There was definite limitation of thoracic motion. The percussion tone was resonant throughout and sibilant rhonci were present at the bases.

A pulmonary roentgenogram taken on August 19, 1950 revealed the previouslv described pattern plus suggestive honeycombing of the upper part of each lung field.

Three days previously the patient had been placed on ACTH therapy. Up to September 7, 1950, the date of hospital discharge, he received a total of 1300 mg. of the drug. A maintenance dose of 20 mg. per diem is currently prescribed.

Roentgenograms taken on September 1 failed to reveal any appreciable change in the pattern. During the period of hospitalization several clinical blood studies and numerous urinalyses failed to disclose significant abnormalities. The temperature range was within normal limits, the pulse ranged between 80 and 100, and the respiratory rate between 20 and 30.

During the 3 weeks of hospitalization the patient developed an excellent appetite and gained 8 pounds. The mental outlook was definitely improved. A decrease in dyspnea and in the frequency of coughing paroxysms was noted.

The latest examination prior to this report was made on October 11. The patient has increased his weight to 132 pounds and his vital capacity to 2.4 L.

Case 2. A white woman, now 70 years of age, was referred in May 1950 for consultation on the basis of pulmonary roentgenogram interpretation.

The history of exposure to beryllium was rather meager. In 1941 she had resided two standard city blocks southwest of a beryllium basic production plant. From 1942

until the present time she has resided eight to nine blocks directly south of the same plant. No history of either direct or indirect contact with workers at the plant could be established. The patient did assert that, when living in the immediate area, she was conscious of fumes which caused coughing, especially at night.

Initial examination was made on May 17, 1949. The history of symptoms dated back to September 1948 with a coryza. The coryza improved but a definite "hoarseness" became apparent which was associated with a slight, "tickling" cough which gradually became productive in the course of several months.

The mucous was tenacious, of yellow color, and devoid of blood. The cough had progressed in severity and frequency and had been paralleled with a progressive dyspnea and a sense of substernal pressure and burning in the inspiratory phase. However the appetite had remained unimpaired and there had been no apparent weight loss.

The temperature was normal, pulse rate 96 and respiratory rate 32. Blood pressure was 150/70. The weight was 169 pounds; height 62½ inches. The vital capacity was read at 1.0 L. and computed at 32 per cent of the estimated norm[illegible]. She exhibited severe dyspnea at rest. Pronounced acrocyanosis was noted. There was no pulmonary osteo-arthropathy.

Definite limitation of thoracic motion was evident. The patient complained of substernal pain on relatively mild inspiratory effort. Percussion tone was resonant throughout. Basal sibilant rhonci were present.

Pulmonary roentgenograms taken on May 18, 1949 revealed a diffuse granular involvement of the lung fields. The pattern indicated a diagnosis of chronic pulmonary granulomatosis. X-rays of the hands did not disclose osseous abnormalities as sometimes seen in Boeck's sarcoidosis.

The patient was examined at rather frequent intervals for progress of the disease. On November 29, 1949 clinical studies on a blood sample showed the following results: red blood count 5,300,000; hemoglobin 100 per cent; white cell count 12,150 with a normal differential; total protein of 7.2 mg. with an albumin globulin ratio of 1.7:1. Urinalysis was essentially negative.

As the patient's symptoms became progressively aggravated hospitalization for oxygen therapy became necessary on May 8, 1950. Until this time her mental outlook had been fairly optimistic and her cooperative spirit exceptional.

Examination on hospital admission revealed a rather well nourished but mentally depressed white woman, 62½ inches in height and weighing 160 pounds. Spasmodic coughing was almost constant throughout the examination. Constant high concentration of oxygen was necessary for the purpose of maintaining some degree of comfort. The respiratory rate was 48 per minute. Despite the oxygen therapy a pronounced acrocyanosis was apparent. The finger nails showed early evidence of "watch-glass" curving. Cardiac dullness was beyond normal limits bilaterally; cardiac rate was 120 and blood pressure 150/82. Thoracic motion was limited. The percussion tone was resonant throughout. Auscultation revealed sibilant inspiratory rhonci throughout. Moist rales were discerned at the bases posteriorly.

A pulmonary roentgenogram taken on May 10, 1950 revealed the same nodular and granular pattern of the parenchyma as previously described. Enlargement of the cardiac silhouette was evident.

Laboratory observations at admission were as follows: red blood count 4,140,000; hemoglobin 80 per cent; white blood count 10,250 with a normal differential; total protein of 10.4 mg. with an albumin globulin ratio of 1.3:1. Numerous urinalyses were essentially negative throughout her hospital stay. On September 27 the red blood count

was 4,520,000, hemoglobin 94 per cent, and white blood count 10,950 with a normal differential.

Approximately 4 Gm. of cortisone was administered between June 4 and 16, without any appreciable clinical response. Almost constant utilization of oxygen was necessary to relieve dyspnea and cyanosis. Due to an appreciable right sided cardiac failure with evidence of decompensation, mercuhydrin and digitalis were administered with some therapeutic response as shown by the disappearance of the peripheral edema.

On July 28 ACTH therapy was instituted. Until the date of hospital discharge 2 months later, she had received more than 3 Gm. of the drug. The patient has been on a daily maintenance dosage of 20 mg. of the drug to date.

In addition to cortisone and ACTH therapy, the patient received 12 million units of penicillin between May 14 and June 3 and also 10 Gm. of chloromycetin between July 24 and August 3. No apparent clinical improvement resulted from the use of the latter two drugs.

Pulmonary roentgenograms taken on August 7 disclosed some improvement. Further roentgen study on September 27 demonstrated additional improvement.

The temperature remained within normal limits throughout the period of hospitalization. The pulse rate ranged between 80 and 100; the respiratory rate between 20 and 40.

A gradual but appreciable clinical improvement was obvious within 2 days from the inception of ACTH therapy. Dyspnea and cyanosis receded. The need for oxygen became less frequent and has not been required since September 20. The mental attitude improved definitely and the patient acquired a rather optimistic attitude toward the future. There was a gradual weight loss despite a normal appetite. Some of this loss may be ascribed to the concomitant loss of cardiac decompensation edema. Weight at the beginning of ACTH therapy was 142 pounds as against a hospital discharge weight of 138 pounds.

Case 3. A 21-year-old housewife was admitted to the Cleveland Clinic Hospital on June 13, 1950, with the complaints of chronic cough, progressive shortness of breath and a 30 pound weight loss in the previous 3 years. She had been essentially bedfast during the last 7 months. The insidious onset, 3 years before, was postpartum and the symptoms were described as progressive and unrelenting. A diagnosis of sarcoidosis had been made elsewhere.

Past history was noncontributory except for the fact that, beginning in May, 1945, the patient had worked for 1 year as a baker on the ovens in a fluorescent tube manufacturing plant.

On initial examination obvious weight loss, cyanosis of the mucous membranes and nail beds, dyspnea at rest, moderate clubbing of the fingers and toes, and fine to medium inspiratory rales over the lower halves of both lung fields were evident, accompanied by a protodiastolic gallop rhythm. The temperature was normal, pulse rate 110, and weight 85 pounds with a height of 64 inches.

Stereoroentgenograms of the chest revealed a generalized fine nodulation with superimposed linear infiltration. The latter made the cardiovascular silhouette difficult to outline. X-ray examination of the hands showed changes in the terminal phalanges suggestive of hypertrophic osteo-arthropathy. The radiologist's interpretation of the chest was chronic berylliosis (chronic beryllium poisoning).

The clinical impression from the above studies was that of chronic beryllium poisoning (chronic pulmonary granulomatosis in a beryllium worker). The following studies were carried out: urinalyses negative in all respects; blood counts normal with the initial count showing 12.0 Gm. of hemoglobin with a white blood count of 6550 with a normal

differential; the blood sugar reading was normal with 93 mg. per cent fasting; Wassermann and Kahn reactions were negative; measurement of serum proteins by Kjeldahl's method showed an increase in the total proteins with a relative hyperglobulinemia, the total measuring 8.1 Gm. with 3.3 Gm. of albumin and 4.8 Gm. globulin; the erythrocyte sedimentation rate was elevated only slightly; multiple sputum examinations were negative on smear and cultural studies for tubercle bacilli, fusespirochetes, fungi and all other pathogenic organisms; neither of 2 electrocardiograms showed diagnostic changes; skin tests with coccidioidin and histoplasmin extracts were negative; the Kveim skin test for sarcoid, applied on June 13, 1950, was negative (with the site of the test being followed by periodic observations for 4 months); patch tests with 1 per cent buffered beryllium fluoride, beryllium sulfate and beryllium nitrate showed from 1 to 3 plus positive reactions. On admission the optimum vital capacity reading on 3 separate tests was 700 cc. (less than 25 per cent of the patient's computed normal). Arteriole oxygen saturation was 74 per cent.

On June 15 a right thoracotomy was performed by Dr. Donald B. Effler, head of the Department of Thoracic Surgery. Dr. John B. Hazard, Pathologist, interpreted the microscopic picture as representative of chronic pulmonary granulomatosis: "Sections reveal an intense inflammatory process, evidenced by pronounced thickening of alveolar walls due to an infiltration of lymphocytes and plasma cells and in addition forming the majority of the bulk in many areas; rather circumscribed collections of histiocytes, giant cells of foreign body type and in some places fibroblasts. Some of the giant cells show vacuolation of their cytoplasm. A connective tissue septum near one margin is of only slightly increased width and contains scattered lymphocytes. Alveolar lumina contain giant cells of foreign body type, occasional collections of histiocytes and pink granular coagulum in which are scattered lymphocytes. Bronchioles show a mucous membrane of usual character with common relationship to smooth muscle. Alveolar epithelium in some of the smaller alveoli which were found in regions of greatest involvement, is formed by cuboidal epithelium rather than usual flat type. There are no areas of caseous necrosis. A small amount of brownish-black granular pigment (carbon) is present in one area. The pleura shows engorged vessels and is infiltrated by moderate numbers of plasma cells, lymphocytes and a few eosinophiles."

Dr. Frank R. Dutra of the Kettering Laboratory of the University of Cincinnati studied a section of the above lung biopsy and agreed with Dr. Hazard that "microscopically the picture is that of beryllium granulomatosis."

Because of respiratory embarrassment and cyanosis, oxygen therapy had been instituted on the patient's first day of hospitalization. On June 21 a course of ACTH was instituted and continued until July 16, having been maintained under appropriate laboratory control and at maximum limits of tolerance. Within 24 hours the patient showed both subjective and objective improvement. Within 48 hours the cyanosis had disappeared and oxygen was discontinued. On June 28 the oxygen arteriole saturation was found to have risen to 85 per cent and within a week to 96 per cent. The vital capacity showed slow but steady improvement, measuring 1.5 L. (1500 cc.) by the time of discharge on July 25.

A second thoracotomy lung biopsy (this time on the left) was obtained by Dr. Effler on July 17. This Dr. Hazard reported as showing no apparent histologic change as compared with the previous biopsy.*

**It is to be emphasized that the quotation of no essential histologic change in the second biopsy after ACTH administration was qualitative. Dr. Hazard is carrying out further study of histologic detail from a quantitative standpoint as the amount of exudate may be quantitatively less in the second biopsy. This further study will be reported subsequently.*

The patient was returned to the hospital on August 3 because of recurrence of initial symptoms in the 72 hours previous to readmission. Her vital capacity was found to have dropped to 1 L. (1000 cc.). Mild cyanosis and the original gallop rhythm had reappeared. ACTH therapy was again instituted with satisfactory subjective and objective clinical response. On August 15 cortisone was substituted for ACTH. However as a mild relapse was observed, this medication was discontinued and ACTH resumed.

The patient was discharged on August 28, on an established 12 hour maintenance level of 8.0 mg. of ACTH. Subsequent ambulatory check-ups have been made and the patient appears relatively symptom-free on moderately restricted activity. Subsequent serial x-rays have shown questionable improvement. Her weight, on dismissal, was 91½ pounds.

Case 4. A 32-year-old housewife was observed at the Clinic on September 14, 1950. For the previous 3 years she had experienced progressive shortness of breath, and for 2 of these a progressive cough and anorexia; during this latter period a 34 pound weight loss occurred. The cough was nonproductive and related to exertion.

Physical examination revealed a patient with normal temperature, regular pulse, and blood pressure of 120/76. The weight was 101 pounds and height 64 inches. Numerous inspiratory fine to medium rales along with sibilant rhonchi were elicited over two-thirds of both lung fields, most evident in the bases.

The referring physician kindly loaned x-ray films and a cervical lymph node biopsy slide which had been made of the patient in March 1950. Dr. John B. Hazard interpreted the lymph node histology as chronic granulomatous lymphadenitis. It was his opinion that chronic beryllium poisoning should be considered in the differential diagnosis.

Roentgenograms taken at this time showed no essential change from those of the previous March; both disclosed generalized fine nodulation characteristic of the pattern observed in chronic beryllium poisoning (chronic pulmonary granulomatosis in a beryllium worker).

Past history revealed that the patient had been employed in a fluorescent lamp plant from March 1942 until March 1944, during which time she had done considerable salvage work.

The maximum vital capacity determination on the original visit was 1.52 L. (with the patient's computed normal estimated at 2.8 L.). The hemoglobin was 15.2 Gm. with a white count of 6950; the cell volume was 48 cc. The urinalysis was negative in all respects. The blood sugar reading was 104 mg. per cent fasting, and Wassermann and Kahn reactions were negative.

She entered the hospital on October 12 for further diagnostic studies. In the interval the patient had experienced a further progression of symptoms, including shortness of breath and paroxysms of nonproductive coughing on limited exertion. Her weight had decreased to 98 pounds.

Additional diagnostic studies were essentially negative, including multiple sputum examinations, Kveim skin test for sarcoid, skin tests with histoplasmin and coccidioidin extracts, and bromsulfalein test of liver function. The serum proteins measured 7.3 Gm., with the albumin 3.9 Gm. and the globulin 3.4 Gm. Patch tests with 0.1 to 1.0 per cent beryllium compounds showed positive reactions varying from 1 to 2 plus which persisted and even increased in reactions to 2 and 3 plus respectively during the remainder of hospitalization.

On October 15 the conclusion was reached that chronic beryllium poisoning existed and ACTH therapy was instituted. The initial dosage was 40 mg. every 6 hours, con-

trolled by appropriate laboratory study; the maximum tolerated dosage was 60 mg. every 6 hours, attained on October 19 and maintained until 3 days prior to discharge when the dosage was reduced. ACTH was discontinued on November 4, and the patient returned home the following day.

During this therapy the patient showed both subjective and objective improvement and a weight of 110 pounds was attained; this, however, was attributed in part to concomitant edema, and at the time of discharge she weighed 105½ pounds. The vital capacity demonstrated a steady increase, having reached 2.1 L.

It was decided to await development in the patient's condition before placing her on a maintenance dosage of the drug. However a recent letter reveals a symptomatic relapse and she has been scheduled for further progress studies. It is anticipated that additional ACTH therapy will be indicated as a maintenance measure.

Summary

1. Four patients treated with ACTH are reported. Each had progressive and disabling chronic beryllium poisoning.

2. At least a moderate degree of temporary improvement has occurred in each case with this therapy. We have obtained no such benefit from any other form of treatment.

3. This report covers only a period of up to 6 months observation with ACTH medication. Prolonged observation is necessary before a final evaluation can be made.

4. ACTH therapy, as demonstrated in these patients, may serve as at least a regressive measure.

ADDENDUM: Since the preparation of the foregoing case reports, 2 additional patients with chronic beryllium poisoning have been treated with ACTH with satisfactory initial response. These further cases will be incorporated in a later report.

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CORRECTION OF SADDLE NOSE DEFORMITIES

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SADDLE NOSE occurs second in frequency to the hump nose deformity among the malformations observed in rhinoplastic practice.

On an etiologic basis saddle nose deformities may be grouped in three broad categories: congenital—a relatively uncommon occurrence; infectious—generally associated with syphilis but often a sequela of pyogenic septal abscess; traumatic—resultant from a direct external blow or the consequence of extensive septal resection.

Despite the etiologic factor involved, these deformities have certain points in common:

1. On the profile projection there is a scapha involving all or a portion of the cephalad two-thirds of the nasal dorsum.
2. On full face observation a real or apparent widening of the nasal dorsum is demonstrated.
3. A decrease of function results due to a decrease in the anteroposterior diameter of the airway.

FIG. 1. Case 1.

Except for the minor deformities which can be corrected by a rearrangement of the existent nasal structures, all corrective procedures are based on the premise of camouflaging the defect by means of some type of implant.

Over the years many substances have been recommended for building up tissue defects. Most of these were incapable of becoming an integral part of the tissues and sooner or later either shifted or provoked sufficient inflammatory reaction to necessitate their removal. The materials that have best withstood the test of time are autogenous cancellous bone, usually obtained from the iliac crest, autogenous rib cartilage, and isografts of rib cartilage preserved

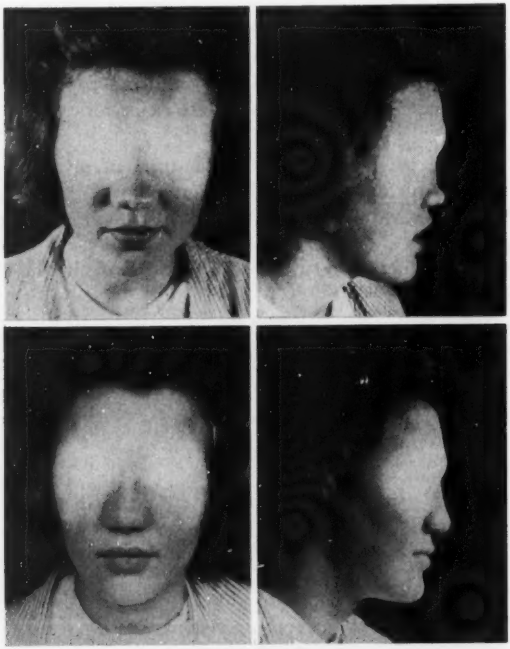

FIG. 2. Case 2.

according to the technic of Pierce and O'Connor. In Case 1, preserved rib cartilage was utilized as the graft material. In Cases 2 and 3 autogenous cancellous bone was the substance of choice.

The bed for the graft in the present series was created through bilateral circumferential vestibular incisions along the caudal margins of the lower lateral cartilages. This type of incision is preferred for several reasons: (1) it has been found adequate for insertion of a graft as large as required to camouflage even the major defects; (2) when a strut is essential for support of the nasal tip, it may be inserted into the columella without recourse to additional incisions;

(3) any necessary modeling of the lower lateral cartilages can be accomplished easily, and (4) there is no externally visible scar.

In constructing the bed for the graft the soft tissues were separated over the nasal dorsum by sharp dissection, thereby preserving a thick layer of skin and subcutaneous tissue which covered the implant and minimized the minor irregularities of its surface.

The 3 cases presented were selected as representative of the three etiologic categories:

Case 1—Congenital cleft nose with associated saddle deformity (fig. 1).

Case 2—Saddle deformity following pyogenic septal abscess (fig. 2).

Case 3—Saddle deformity due to direct trauma (fig. 3).

FIG. 3. Case 3.

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RUBBER TUBE IN COMMON BILE DUCT FOR TWENTY-FIVE YEARS

A Case Report

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THE following case report is believed to be of unusual interest because a rubber tube remained in the common hepatic duct of the patient for more than 25 years before it resulted in any appreciable symptomatology.

Case Report

A 57-year-old bartender was first examined at the Cleveland Clinic in January 1950 because of attacks of chills, fever, and mild intermittent epigastric pain of 4 months' duration. There had been a weight loss of approximately 20 pounds during the same

FIG. 1. Retrograde pyelogram, right. Radio-opaque rubber tube is shown just medial to shadow of renal pelvis.

FIG. 2. Longitudinal view of calculus-encrusted rubber tube.

period. The patient thought he had detected blood in the urine on several recent occasions.

The past history included typhoid and malaria in childhood, syphilis in 1914 and gonorrhea in 1927. He had a cholecystectomy for gallstones in 1924 in another city. Fortunately, the other hospital keeps excellent records, and the following data concerning the operation are available:

The patient, then aged 32 years, entered the hospital on September 12, 1924, complaining of abdominal pain which had persisted for 3 days. Physical examination was negative except for the presence of tenderness and rigidity in the right upper quadrant of the abdomen. The urine was normal. A diagnosis of acute cholecystitis was made and operation performed a few hours after admission. The abdomen was opened through a vertical incision and the gallbladder wall found to be thickened, dark red in color with purple and gray patches. A stone could be felt in the region of the cystic duct. What was taken to be the cystic duct was divided, but it was recognized immediately that the common duct had been divided instead. The true cystic duct and cystic vessels were then identified and divided, and the gallbladder removed. The divided common duct was repaired over a rubber tube with interrupted sutures of fine catgut. The common hepatic duct was drained. The abdomen was drained and the wall closed. The pathologist reported active, chronic purulent cholecystitis with cholelithiasis. An x-ray of the abdomen taken on the fourteenth postoperative day showed the rubber

FIG. 3. View of cross-section of calculus showing lumen of rubber partially preserved at this point. (The ends were occluded.)

FIG. 4. X-ray of removed specimen showing rubber tube in center.

tube slightly to the right side of the spine and well below the liver shadow. The patient was discharged on the fifteenth postoperative day after a satisfactory convalescence.

Prior to the present illness the patient's health had been excellent except for mild postprandial bloating and belching, and episodes of painless vomiting once or twice a year which persisted for a day or two. There had been no jaundice, severe abdominal pain, food intolerance, change in bowel habits or alterations in the character of the stool.

Physical examination: Temperature was 98 F., pulse 76 and blood pressure 100/70. The patient was a tired-appearing, chronically ill man. The skin was swarthy. There was questionable icterus of the sclerae. The heart and lungs were normal. A well-healed scar was noted in the right upper abdomen. The liver edge was palpable 4 cm. below the costal margin and was regular, sharp and firm. The spleen was not palpable. There were small external hemorrhoids and moderate prostatic enlargement.

Laboratory data: Leukocyte and erythrocyte counts and hemoglobin determinations were within normal limits. Urine was negative except for a few pus cells in one of several specimens; the urine culture was sterile. The blood Wassermann and Kahn tests were negative. The sedimentation rate was elevated to 2 mm. per minute (normal 0.5 mm. per minute). The bromsulfalein retention was 24 per cent, 40 per cent and 40 per cent (normal 10 per cent) on three occasions. The cephalin flocculation test was negative and the icterus index was 10 units (normal to 8). The indirect serum bilirubin test was 2.7 mg. and 2.0 mg. on two examinations (normal to 1.5 mg.).

X-rays: The chest was normal. KUB examination showed a radio-opaque tube in the right upper quadrant. Esophagus, stomach, duodenum and colon were normal by barium study. A right retrograde pyelogram made at the time of cystoscopy was also normal, and showed that the tube was not related to the kidney (fig. 1).

Operation: The abdomen was explored on March 14, 1950 after excision of the old operative scar; gas-oxygen ether endotracheal anesthesia was used. There were dense adhesions but the calculus was readily palpated and exposed in a greatly dilated common duct. The lumen of the common duct was almost completely occluded by the cigar-shaped calculus containing the rubber tube in its center (figs. 2, 3 and 4). The

calculus was removed easily and a T tube inserted into the common duct. The abdomen was drained and closed with wire sutures and skin clips.

The removed specimen was described as follows: "A hard mass of black and yellow mottled color, which measured 6.5 by 1.5 cm. in greatest diameter. Cross sections reveal a central red rubber catheter with partly obliterated lumen."

Convalescence was smooth except for deep induration about the operative wound suggesting an intra-abdominal inflammatory mass; this condition was unaccompanied by fever, and ultimately subsided. Cholangiograms on the ninth postoperative day were normal although the common duct was still dilated (fig. 5). The T tube was removed on the eleventh postoperative day and the patient discharged 3 days later. When last seen in June, 1950, nearly 3 months after the operation, the patient was well except for mild constipation. He had regained his preoperative weight and was planning to return to work. Liver function tests were normal as shown by a bromsulfalein retention of 6 per cent, a negative cephalin-flocculation test, a thymol turbidity of 1.2 units, serum albumin 4.2 Gm. and serum globulin 2.4 Gm.

Comment

The foregoing case exemplifies the advantage of prompt recognition of a terrifying accident—the division of the common duct—with appropriate repair carried out at the time of the injury. Physicians familiar with the course

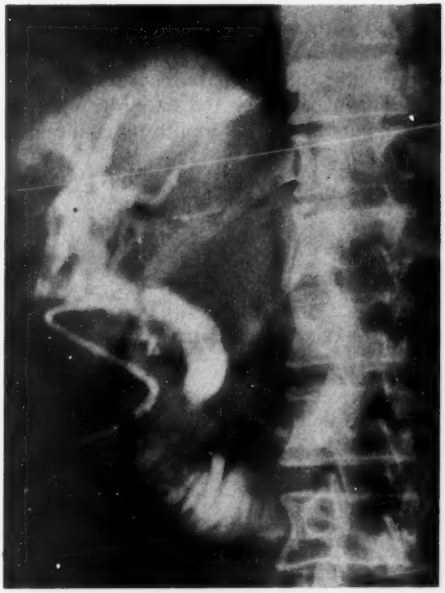

Fig. 5. Postoperative cholangiogram. Common duct still dilated but unobstructed; foreign body has been removed.

of "biliary cripples" who so often require repeated plastic procedures for a damaged common duct, will accept a 25 year "cure" as an excellent result. A rubber tube used as an internal splint for a repaired common duct usually will pass spontaneously, and it must be regarded as "hard luck" rather than poor management that the one used in this patient did not. It is noteworthy, however, that the common bile duct could retain a foreign body for such a long time before causing the host any appreciable difficulty. Finally, the case demonstrates that the common duct may be occluded almost completely by a foreign body without the development of clinical jaundice. The symptoms which did develop were undoubtedly the result of recurrent cholangitis and partial hepatic insufficiency. It may be that the "red urine" which the patient noted on two or three occasions actually represented bile in the urine, and that his naturally dark complexion obscured the other manifestations of a transient jaundice. Although the follow-up is short, the absence of symptoms and the apparent return of normal liver function suggest a good prognosis.

Summary

A case is reported in which an accidental division of the common bile duct occurred during a cholecystectomy for acute cholecystitis more than 25 years previously. It was repaired immediately, and the surgeon utilized a short length of rubber tube as an internal splint. The tube failed to pass and ultimately became encrusted with sufficient calcareous deposit nearly to occlude the duct. Nevertheless, disabling attacks of cholangitis did not occur for 25 years, nor did an irreversible biliary cirrhosis develop. Operative removal of the large calculus which formed over the tube was easily effected, and the patient appeared to be in good health 3 months after the second operation.

ANNOUNCEMENTS

Appointment

Dr. F. Mason Sones, Jr. has been made a member of the permanent staff in the Department of Cardiorespiratory Disease. Dr. Sones graduated from Western Maryland College in 1940 and from the University of Maryland School of Medicine in 1943. He interned at the University Hospital in Baltimore. During 1944 to 1946 he served in the Medical Corps of the U. S. Army Air Force, after which he spent 3 years as resident at Henry Ford Hospital. His residency included 2 years in Internal Medicine and 1 year in Cardiology. In 1949 Dr. Sones was appointed to the Staff in Pediatric Cardiology at Henry Ford Hospital, which position he occupied until his appointment at the Cleveland Clinic in October, 1950.

Bunts Course

The Frank E. Bunts Educational Institute announces a course in General Surgery with emphasis on surgery of the gastro-intestinal tract, on May 3, 4 and 5, 1951. A complete program will be published in the April issue of the Quarterly.

Erratum

As a result of a statistical error on pages 212, 213 and 215 of the October 1950 Quarterly, the total series of colon resections was reported as 274 instead of 234.